THE AMERICAN REVIEW OF TUBERCULOSIS

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ABSTRACTS OF TUBERCULOSIS

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Teaching of Tuberculosis.—During the year 1930, in the public clinics of five large cities, 11,782 individuals were diagnosed for the first time as having tuberculosis. Statistics showed that in 70 per cent of these patients the disease had progressed to a stage, moderate or far advanced, lessening the opportunity for recovery. The community likewise had been subjected to the possible hazard of uncontrolled infection. The blame for much of this delayed diagnosis must rest with either a lack of response on the part of patients to lay education, or with a lack of ability on the part of many physicians to diagnose tuberculosis in its early stages, or a combination of both. Questionnaires were sent to 66 approved colleges in the United States which offer a complete curriculum in medicine. Sixty-four of these colleges returned their questionnaires more or less completely filled out. Nineteen colleges, or 29.7 per cent, have a special department for teaching tuberculosis. Thirty-three colleges, or 51.6 per cent, have availed themselves of the special knowledge in teaching tuberculosis to their students. This is an important consideration. Nine additional colleges, or 14.1 per cent of the total, have teaching in tuberculosis divided between the internist and a tuberculosis specialist. The college faculty having representatives on the specialty services of tuberculosis sanatoria number only thirty-seven, or 57.8 per cent. Eleven colleges reported resident clerkship affiliations of varying lengths of time. Statistics show that only 9 of the 64 medical colleges offer regular postgraduate courses. There is a definite lack of facilities for postgraduate instruction for that large group of medical practitioners about to graduate or for those who have been in practice for many years. The colleges with special tuberculosis departments, numbering nineteen, have failed to appreciate this great need, for only one of this number offers a postgraduate course. The undergraduate teaching of tuberculosis in German universities has not been stressed to any considerable extent. A chair of tuberculosis does not exist in any German university. The lectures on tuberculosis do not take place at regular intervals. They also are usually limited to pulmonary and surgical tuberculosis and therapeutic methods. A great number of the universities arrange medical trips once or twice a year to visit sanatoria and inspect their work. Postgraduate teaching of tuberculosis in Germany was stressed long before it was in other countries and a good organization was developed for instruction to the medical practitioner. All the

universities organize regular postgraduate courses for physicians, which include tuberculosis. There are, however, a few universities which have organized special courses in this disease. In Italy, Holland, Norway, Austria, Poland, Rumania and Sweden, postgraduate courses are given with regular and irregular frequency. The limited number of such courses given in these countries fails to emphasize the importance of the tuberculosis problem. Great Britain does not manifest the interest in postgraduate teaching that is in evidence on the continent. The European method places its main emphasis on postgraduate study. In contradistinction, a plan developed by the author stresses the undergraduate as well as the postgraduate instruction. Special attention is directed to undergraduate teaching through the resident clerkship. Postgraduate teaching involves a systematic program of fellowships.—*Medical Teaching in Tuberculosis, B. Goldberg and J. S. Whitney, J. Am. M. Ass., August 27, 1932, xcix, 707.*—(*G. L. L.*)

Compensation for Pulmonary Disease.—A short account of the regulations in Great Britain governing the compensable diseases, silicosis and asbestosis, as such, or either of these diseases, when accompanied by tuberculosis, shows that compensation is made through a system of so-called schemes that are defined and regulated by law. The mere fact that a claimant is suffering from one of the diseases does not entitle him to compensation unless he has worked in an industry or process included in one of the schemes. The scheme provides for the authority of the medical board and for the finances. The medical board deals with applications for compensation and makes periodic examinations. Fees are collected from applicants for certificates and from employers when claims are successful and also from employers of workers who undergo periodic examinations. Each industry or process has its own modification of the basic scheme. The refractories industries cover the processes of getting silica rock or ganister and the manufacture of silica bricks. These are used for lining furnaces, but the fire-clay industry is not covered unless the clay contains 80 per cent silica. After a periodic examination a worker may be suspended if he is found to have silicosis or tuberculosis or both. Men over 45 years old may continue work if they have silicosis only and have worked for 20 years in the industry. All claims are dealt with by a joint committee and no cases are decided in court. A compulsory levy of 6.25 per cent of each worker's wage is made by employers to cover allowed claims. The sandstone industry has similar regulations but, unless the sandstone contains 50 per cent silica, the workers are not admitted to the scheme. The wage-levy of the workers varies with the type of work done. It is highest for stone-dressers and masons. The various-industries scheme applies to other workers in silica. The workers in these are not periodically examined but, with the exception of certain pottery processes, partial disability is at times allowed. In foundries the workers carried in this scheme are those who handle bricks containing 80 per cent silica, those freeing steel-castings from adherent sand, and sand-blasters. In tin-mining the scheme applies only to those who crush the ore and rock. The metal-grinding industries scheme is similar to the various-industries scheme. The asbestos-industry scheme is also similar, but periodic examinations are required.—*Workers Compensation in Pulmonary Disease, C. L. Sutherland, J. State Med., December, 1932, xl, 709.*—(*J. F. B.*)

Appropriations for Dispensary Service.—In the past the London County Council has contributed 25 per cent toward the net approved expenditure incurred by the metropolitan borough councils on the tuberculosis dispensary service provided by them. It now proposes to substitute a block grant system. The grant is to be based on the latest available figures of actual expenditure, with such modifications to meet anticipated variations in future cost as may be determined. Before the metropolitan borough councils may reduce or expand the service or facilities, the consent of the County Council must be obtained.—*London Tuberculosis Dispensary Service, Brit. M. J., November 19, 1932, no. 3750, 940.*—(*T. O. R.*)

Prognosis in Dispensary Work.—This study is based on 6,777 persons examined in the dispensary at Bremen in 1928. Of these, 4,734 were healthy, 794 had open and 741 closed pulmonary tuberculosis; 171 had extrapulmonary tuberculosis and 329 had nontuberculous diseases. The tuberculous patients were observed to the end of 1931. Healed were 22.2 per cent of closed, and 8.0 per cent of open cases, while 4.0 and 38.6 per cent, respectively, died. Of the closed cases, 13.8 per cent became open, most of them belonging to a group which was initially classed as prognostically unfavorable. The initial prognosis in the open group was correct to the extent that according to the three prognostic classes used, the mortality was 9.6 per cent in the most favorable group and 76 per cent in the unfavorable group. In regard to mortality, general course and improvement, the initial prognoses were fairly correct in a statistical way for whole groups

of patients, but a considerable number of errors occurred in regard to individual patients. The fate—healing or death—is usually decided within five years for open cases. That a patient remains open for a long period of time is a rather rare occurrence. Out of 1,200 open patients, only 25 are known to have been open for ten years or more. There were 210 patients who had an exudative pleuritis or its residua not associated with parenchymal lesions; of these only 5 developed pulmonary lesions during the observation period. In the group of 4,734 persons, originally diagnosed as healthy, 118 developed tuberculosis within the three years, among them 43 children. In 93 of these patients, the lesions were evidently of recent development.—*Wie bewährt sich die Prognose in der Fürsorge? H. Grass and F. Hoth, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 43.*—(*M. P.*)

Tuberculosis-Care Committees.—These committees serve the tuberculosis patient in London by (1) helping the families readjust their lives, (2) providing extra food or clothing for the patient, (3) adjusting insurance problems, and (4) more recently by organizing handicrafts classes which enable the patients to earn enough to supply their own comforts.—*The Work of Tuberculosis Care Committees, M. T. Kelly, Brit. J. Tuberc., January, 1933, xxvii, 19.*—(*R. D.*)

Tuberculosis in Tennessee.—The Tennessee program of control of tuberculosis as an activity of the state government had its beginning in 1927. The program has been essentially one of field activities, and during the first four years since its inauguration 1,794 clinics have been held, 28,131 examinations made, and 5,243 positive cases of tuberculosis found and brought under the active direction of their personal physicians. At the time the program was started, the death-rate from tuberculosis in Tennessee was 144 per hundred thousand population, constituting a definite challenge to the health agencies. In 1931 the tuberculosis death-rate from tuberculosis (all forms) was 109 (about 97 for pulmonary tuberculosis alone). Special field studies of tuberculosis have been in progress during the past two and one-half years. Some of the findings in these studies indicate (1) the importance of household contact in the spread of tuberculosis and (2) the importance of chronic fibroid cases in the spread of tuberculous infection in the state. During the first year Gibson County was studied, an area predominantly agricultural, with about one-fourth of the inhabitants of the Negro race. Here the death-rate from tuberculosis in age-groups over 40 in the white population was found to be markedly elevated over that of the United States registration area as a whole. Also, the maximum death-rate from tuberculosis occurs in an older age-group than in the United States registration area. These differences can be shown also to hold for the state as a whole. Tuberculin testing of school children showed positive reactors to constitute 56 per cent in the age-groups from 5 to 19 years. This, for a rural area, indicates a marked prevalence of infectious cases in Tennessee. Careful family and individual epidemiological histories were assembled on home visits to 265 tuberculous families and all available family data recorded. Well over one-half (59 per cent) of all deaths of white persons from tuberculosis were in those over 40 years of age, while in the colored race only 22 per cent were in those over 40. There was a history of tuberculosis in one or both parents in 39 per cent of the 111 basal cases in white persons and in 35 per cent of the 106 basal cases in colored persons. These findings afford good evidence regarding the importance of the parent as a primary focus of infection. The effect of household association with cases of tuberculosis was also studied. One thousand and ninety-five such associates were examined. In the age-group under 5 years about one-half of those examined in the clinics exhibited some evidence of tuberculous infection. Eighty-five per cent of adults associated were found infected. In every age-group the proportion of infections was higher in the colored than in the white race. The study was further carried on in Kingsport, an industrial city of 15,000. About 600 Negroes were resident in this community, and practically every Negro had a complete examination, including roentgenological study. Nearly 10 per cent were found to have definite or suspected adult types of tuberculosis (4 per cent definite, 6 per cent suspected). The positive results with tuberculin testing were 13 per cent in the age-group under 5 years, 61 per cent in the 5- to 9-year group, 75 per cent in the 10- to 14-year group and 90 per cent in those over 15 years. The logical means of approach in the control of tuberculosis in Tennessee, in the light of information now at hand, would seem to centre around the breaking of the chain of long-continued contact between patients with fibroid and other types of tuberculosis with their household associates. Eventually this would mean the establishment of hospitals or retreats for the care of the patient who is spreading tuberculous infection among members of the family and friends.—*Tuberculosis in Tennessee, E. L. Bishop and H. C. Stewart, J. Am. M. Ass., July 30, 1932, xcix, 356.*—(*G. L. L.*)

Tuberculosis Mortality in Germany.—The most potent cause of the decrease in the mortality from tuberculosis is, aside from improved living standards and scientific progress in the field of tuberculosis research, the German social health-insurance scheme which furnishes the basis for increased medical care of the population. Remarkable and partly unexplained is the fact that the mortality from tuberculosis has continued to decrease in spite of depression and unemployment. Epidemiologically the fact of smaller families has played a rôle in this mortality rate during the last decade.—*Über die Ursachen des Rückganges der Tuberkulosesterblichkeit in den Kulturländern, G. Wolff, Deutsche med. Wchnschr., November 18, 1932, lviii, 1844.*—(*H. S. W.*)

Tuberculosis in Latin America.—Two facts are well known about tuberculosis in Latin America: first, tuberculosis mortality is very high; second, little or nothing has been done so far in these countries to control the disease. A table gives some idea of the tuberculosis mortality, although the reported figures are very deficient, particularly in rural areas. In Bolivia, Colombia, Costa Rica, Chile, Ecuador, Salvador, Porto Rico and Venezuela, the mortality from tuberculosis continues to increase; in the other countries the diminution has been insignificant. In Haiti, according to autopsy observations by Choissier, 26 per cent of all deaths are due to tuberculosis. The total number of cases of tuberculosis is unknown, but on the basis of 8 to 10 cases of tuberculosis for each death cases have been roughly estimated as 150,000 (Foster) and 200,000 (Viton) in Argentina; 300,000 (Freytas) in Brazil; 23,000 to 40,000 in Rio de Janeiro; 33,000 in Colombia; 3,000 in Costa Rica; 7,600 in Cuba; 60,000 in Chile; 142,000 in Mexico; 3,800 in Paraguay; 43,000 in Porto Rico; and 23,000 in Uruguay. The number of beds available for tuberculous patients, the minimum of which should be one bed per death per annum, actually is 0.08 in Argentina, 0.042 in Brazil, 0.14 in Costa Rica, 0.49 in Cuba, 0.09 in Chile, 0.2 in Salvador, 0.08 in Mexico, 0.1 in Paraguay, 0.62 in Uruguay. Bolivia, Colombia, Venezuela, Ecuador, Guatemala and Haiti have none. Some steps that have been taken in the prevention and control of the disease in Europe and the United States are enumerated, and the results obtained illustrated; these methods should be tried by the Latin American countries.—*Editorial, Boletin de la Oficina Sanitaria Panamericana, March, 1932, xi, no. 3.*—(*A. V.-M.*)

Tuberculin Studies in Peru.—Pirquet and intracutaneous tests in 800 children in Lima, performed by Nicolas, are analyzed. Of children up to 3 months of age, none reacted; 3 months to one year, 3.1 per cent; 1 to 2 years, 9 per cent; 3 to 5 years, 40.0 per cent; 5 to 10 years, 61.5 per cent; 10 to 15 years, 75.0 per cent. Up to 10 years of age the number of reactors among boys and girls was about the same; after this age the boys reacted in greater numbers. Thirty-three per cent of 389 boys and 29.8 per cent of 402 girls gave positive reactions; 28.9 per cent of 290 children with a history of tuberculosis in the family but living in hygienic surroundings reacted to tuberculin, while 31 per cent of 272 children with no history of tuberculosis in the family but living in contact with tuberculous persons were positive; 28.9 per cent of 238 children with no history of tuberculosis and in perfectly hygienic surroundings, but suffering from other diseases, also were positive. In the rural districts only one per cent of the children were positive reactors, in the summer resorts near Lima 5 per cent, in the new subdivisions 8 per cent, but in the poor and crowded districts 70 per cent.—*C. F. Krumdick, Cronica Medica, July, 1931, xlviii, 226.*—(*A. V.-M.*)

Renal Tuberculosis in Chile.—In the *Hospital de Menores de Valparaiso* 4 cases of renal tuberculosis were observed in 58 autopsies in children less than 2 years old, or 6.89 per cent; and among 281 cases of surgical tuberculosis in children of the same age 4 cases of renal tuberculosis were found, or 1.42 per cent. Nine other cases are reported, concluding that renal tuberculosis in children less than 2 years of age is a surgical condition and as such it should be treated by the urologist.—*Tuberculosis Renal en Chile, E. Grove and E. R. Aldunate, Med. Mod., October, 1931, v, 103.*—(*A. V.-M.*)

BCG.—Two hundred and eighty doctors who had used *BCG* in children of their own families between 1924 and 1932 replied to a questionnaire. The collected data cover observations in 514 children, of whom 60 have certainly lived in contact with tubercle bacilli. Up to September 15, 1932, only 7 of the children had died, and only one of these was possibly tuberculous. Four of the children were ill; the remaining 503 were apparently all well. All of the 280 doctors considered *BCG* harmless, and 118 reported vaccinating 7,017 infants in addition to those in their own families. It is hoped that the confidence of these doctors will convince other practitioners and lead to a wider acceptance of the vaccine.—*On Preventive Vaccination against Tuberculosis with BCG, as Practised by Doctors in Their Own Families, A. Calmette, Brit. J. Tuberc., January, 1933, xxvii, 1.*—(*R. D.*)

Pathogenicity of *BCG*.—When living microörganisms are used for the purpose of vaccination it is important that they should not produce lesions of a progressive character. According to its originators the particular bacillus of tuberculosis, known popularly as *BCG*, is definitely and permanently innocuous, if certain requirements be met with in its cultivation. The question of the avirulence of *BCG* as a fixed character has been recently the subject of considerable investigation. The reports of Watson, Petroff, Kraus and others would indicate that under certain conditions evidence of pathogenicity may occasionally occur in experimentally exposed animals. On the other hand, many investigators have confirmed Calmette's findings. It is pointed out by Petroff that all control of the environment of the organism is lost when it enters the animal body. Hence, a microörganism intended for vaccination should maintain a condition of avirulence regardless of various environmental influences to which it may be exposed. It therefore becomes exceedingly pertinent to know something of the biological behavior of *BCG* after the growth on culture media different from those approved by Calmette. Sasano and Medlar, and Dreyer and Vollum claimed to have obtained virulent strains by culturing on media other than those required by Calmette. Boquet repeated the work of Sasano and Medlar but was unable to confirm their results. The present article deals with results from growing *BCG* on a glycerinated egg-yolk medium. The strain studied was obtained from Calmette and first grown on the required glycerinated broth-potato medium for nine months. The original culture was nonpathogenic for guinea pigs. The culture was then grown for 15 generations on inspissated egg-yolk containing approximately 3 per cent glycerine. Transfers were made each month, for on this medium it grew luxuriantly. With the exception of the first subculture, 4 guinea pigs were inoculated with heavy suspensions prepared from each of the respective subcultures. Each lot of 4 animals was injected as follows: 2 intracerebrally (0.4 cc.); 1 subcutaneously and 1 intraperitoneally (1.0 cc. each). After inoculation the guinea pigs were housed apart to protect from inadvertent exposure to tuberculosis. The inoculated animals were permitted to live for a period of from six months to one year unless they died. At the time of autopsy portions of the principal organs were prepared for section regardless of whether or not there was gross evidence of disease. Attempts were also made to culture acid-fast bacteria that might have been present. Ordinarily only one tissue from each animal was used for cultural purposes. The cultural procedure followed was to treat portions of the emulsified tissue with 5 per cent oxalic acid and seed the material on glycerinated egg-yolk media. In some instances guinea pigs were injected intracutaneously with O. T. In no instance was a typically positive reaction obtained. Although gross lesions of a tuberculous character were not discernible at autopsy, significant lesions were found by subsequent microscopical study in 11 of the animals; 9 of these had been inoculated intracerebrally, 1 subcutaneously and 1 intraperitoneally. In 6 instances in which the bacteria had been introduced into the brain, multiple and well-defined tuberculous lesions were present in the spleen and in the brain. No lesion was considered tuberculous unless acid-fast bacilli could be demonstrated in stained histological sections, or acid-fast bacilli obtained in cultures prepared from tissue containing the lesions. Three of the 11 animals lived only fourteen days; 1 twenty-six days; 3 from thirty-one to thirty-four days; and the rest up to seventy-four days. All died spontaneously. The generation of subculture on glycerine-egg-yolk, producing microscopical lesions, ranged from the fourth to the fifteenth (subcultures 4, 5, 7, 8, 14 and 15). It must be borne in mind that the remaining subcultures produced no demonstrable lesions of tuberculosis. Not all the animals of each lot that were inoculated manifested tuberculous lesions even though one or two may have. The reason why lesions developed in some animals and not in others cannot be satisfactorily explained. The lesions (microscopical) of both the brain and the spleen were indistinguishable from those of comparable duration in these organs following the experimental introduction of virulent mammalian strains of tubercle bacilli. The histopathology was typically that of an early progressive tuberculous process with little if any evidence of a significant inhibitory mechanism. Several attempts were made to transmit the disease to other animals (guinea pigs and rabbits) by inoculation of emulsions of tissues of animals that had died, or inoculation of pure cultures of acid-fast bacilli obtained from the organs of animals possessing lesions of a significant character. Though these attempts were unsuccessful, the fact remains that the particular strain of *BCG* studied, when introduced into guinea pigs in large amounts, not infrequently incited a tissue reaction of a tuberculous character that apparently resulted in death. This study emphasizes the necessity of the examination of properly stained histological sections before a decision is made on the tuberculous or nontuberculous content of a tissue. *Con-*

clusions: The particular strain of *BCG* studied is not devoid of pathogenicity for guinea pigs, and the assertion that the organism is innocuous can not be accepted without reservations. Subculturing the organism on glycerinated egg-yolk medium did not markedly enhance its virulence.—*A Study of the Pathogenicity of the Bacillus of Calmette-Guérin (BCG), W. H. Feldman, Am. J. Path., November, 1932, viii, 755.—(J. S. W.)*

Tuberculosis in Lübeck's Infants.—The infants in Lübeck who developed tuberculosis following vaccination have probably received very different amounts of virulent tubercle bacilli, since some of the infants showed practically no symptoms, while others died from a grave and rapid disease. The length of the incubation period varied considerably. The oral infection produced disease of the cervical lymph nodes, but a primary lesion of the tonsils or in the nasopharyngeal space was only rarely recognizable. A primary tuberculosis of the middle ear occurred relatively frequently. Several cases showed peritonitis through perforation of intestinal ulcers, fatal haemorrhages and chronic ileus. In the absence of such accidents, interstitial tuberculosis produced but little symptoms. Diarrhoea was not a predominant symptom. The most important sign was an enlarged spleen. The most frequent cause of death was generalization. Meningitis occurred 17 times among 68 cases. No infant died after the completion of the first year.—*Beobachtungen bei den Lübecker Säuglingstuberkulosen, H. Kleinschmidt, Beitr. Z. Klin. d. Tuberk., October, 1932, lxxxi, 287.—(M. P.)*

Tuberculosis in Lübeck's Infants.—All infants who died following the vaccination showed tuberculosis, but the extent of the disease varied greatly. There were cases with a small isolated primary complex and finally cases with massive generalized lesions. Following oral infection, it was found that primary lesions occurred in intestines in 98.3 per cent, in the middle ear and in the nasopharyngeal space in 78.3 per cent, in the oesophagus and stomach in 18.3 per cent, and in the lungs in 20 per cent. These findings contradict Calmette's theory that all tuberculous infections start with a silent intestinal lesion. Manifestations of healing were found in the form of calcification of lymph nodes, beginning on the fifty-eighth day and with fair regularity after one hundred and forty-four days.—*Beobachtungen bei den Lübecker Säuglingstuberkulosen, P. Schürmann, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 294.—(M. P.)*

Pasteurization and Nutritive Properties of Milk.—As cow's milk is not a natural food for man, the changes resulting from pasteurization may even be an improvement. The known changes include a 6 per cent increase in the insoluble calcium, a 20 per cent reduction in the iodine content, and a reduction of the vitamine C. The change in the calcium makes cow's milk approximate human milk more closely. The reduction in vitamine C is unimportant, since the supply from milk must be supplemented in any event. There are no experiments to indicate that pasteurized milk is less nutritive to the young child than raw milk. On the contrary, wide clinical experience shows that heated milk has been consumed for years by infants and young children with no detectable deterioration in their nutritive condition. This clinical evidence is worthy of the highest consideration.—*The Effect of Pasteurization upon the Nutritive Properties of Milk, W. G. Savage, Lancet, February 25 & March 4, 1933, ccxxiv, 429 & 485.—(R. D.)*

Aetiological Factors in Development of Tuberculosis.—Infection with the tubercle bacillus is widespread; development of the disease depends on other factors. The incidence of tuberculosis is apparently greater in the nursing staff of general hospitals than among nurses in sanatoria; long hours of duty and lack of fresh air are here prime causes of breakdown. The freedom from tuberculosis noted among 400 children in the Papworth and Preston Hall Tuberculosis Settlements, despite their heredity and their continuous contacts, indicates that an adequate diet, a proper balance between rest and exercise, and a sufficiency of fresh air protect against tuberculosis. Faulty nutrition during the war resulted in a lowered resistance to tuberculosis and is doubtless an important factor at all times. Muscular overexertion and long periods of hospital residence apparently predispose to the development of the disease. —*Causal Factors in the Development of Pulmonary Tuberculosis, J. Watt, Brit. J. Tuberc., January, 1933, 13.—(R. D.)*

Heredity in Tuberculosis.—During the last three years, 125 twins, either tuberculous or from tuberculous surroundings, have been examined. There were 60 pairs of twins in which each showed tuberculous changes, 44 pairs in which only one showed tuberculous changes, and 21 pairs in which none had tuberculosis. In order to establish whether genotypical or environmental conditions are more important in the pathogenesis of tuberculosis, the group of identical and the group of nonidentical twins were compared. In 36 identical twins, 69 per cent showed the same

response to tuberculosis; in 68 nonidentical pairs, 25 per cent behaved in a similar way. It is concluded that the hereditary factor plays a predominant rôle in the pathogenesis and course of tuberculosis.—*Erbuntersuchungen an tuberkulösen Zwillingen, K. Diehl, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 223.*—(*M. P.*)

Hereditary Aspects of Tuberculosis.—Based on Norwegian statistics over long periods of time, the conclusion is reiterated that tuberculosis is a disease which is essentially conditioned by family and heredity. There is a definite change in the character of tuberculosis, a loss of virulence caused by an increase in the resistance of the host or by an adaptation.—*Fortsetzung meiner Studien über Tuberkulose als Generationskrankheit, K. F. Andvord, Beitr. z. Klin. d. Tuberk., December, 1932, lxxxi, 668.*—(*M. P.*)

Tuberculous Twins.—In 125 pairs of twins, mentioned in the preceding paper, correlation factors were calculated for their behavior, dependent on heredity and environment. Analyses of constitutional types yielded essentially negative results, but since the general response to tuberculosis seems to be closely dependent on hereditary factors according to these studies, it is concluded that there must exist a specific hereditary disposition to tuberculosis which is not manifested in recognizable anatomical peculiarities. According to the studies on twins, the hereditary fixation is of approximately the same order as that of schizophrenia.—*Erbuntersuchungen an tuberkulösen Zwillingen, O. v. Verschuer, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 227.*—(*M. P.*)

Exogenous Infection.—When roentgenographical methods are used for the recognition of tuberculous lesions of the lungs in husbands and wives in contact with a tuberculous consort, exogenous infection of adults is clearly demonstrable. Data are given on tuberculous married couples who were observed with varying completeness during periods up to eight years. The study includes observations on latent lesions which, being unaccompanied by manifest symptoms or physical signs, preclude the selective examination of those affected. The number of married couples studied of whom one or both consorts suffered with tuberculosis was 533; 366 were white and 157 negro. Tables are given to show the occurrence of tuberculosis in white wives and husbands after its appearance in the other marital partner. The frequency of infection in wives exposed to husbands with tubercle bacilli in the sputum was 35.5 per cent; in those exposed to husbands with no demonstrable tubercle bacilli 22.9 per cent. The incidence of infection to husbands exposed to wives with open tuberculosis was 45.6 per cent, and when there were no tubercle bacilli in the sputum it was 35.9 per cent. Latent apical tuberculosis, like clinically manifest tuberculosis, was more frequent in husbands than in wives exposed to the disease. As with manifest pulmonary disease, the relation of the latent apical lesion to infection is shown by its greater severity and frequency in persons exposed to partners with tubercle bacilli in the sputum than in those whose partners were not known to have had tubercle bacilli in the sputum. The number of married couples of the negro race under observation has been too small to give satisfactory information concerning the incidence of tuberculosis in the marital partners of tuberculosis persons of this race.—*Exogenous Tuberculous Infection of Adults: Marital Tuberculosis, E. L. Opie and M. F. McPhedran, Arch. Int. Med., December, 1932, l, 945.*—(*W. I. W.*)

Exogenous Reinfection.—These statistical studies on exogenous infection have been made in the city of Gelsenkirchen with a population of 340,000. The districts under investigation had a population of 73,000. The studies extended over a ten year period from 1920 to 1930. A total of 991 cases with open pulmonary tuberculosis was observed. The number of people living in residential contact with these cases was 3,399. During the observation period, 546 new cases were found among the 3,399 exposed persons, that is, 16 per cent. Arranged according to age-groups, the following percentage of each group acquired clinical tuberculosis, living in contact with open cases: 10 per cent of adults, 16.5 per cent of adolescents, 23.2 per cent of school children, 26 per cent of preschool children, and 19.8 per cent of infants. Among the newly contracted diseases, there were 2.4 per cent of tuberculous meningitis, 2.5 per cent of tuberculosis of the bones and 22.5 per cent of open pulmonary tuberculosis. The analyses showed that a period of several years may intervene between the beginning of the contact and of the appearance of clinical disease. Not all the 991 cases of open pulmonary tuberculosis could be accused of having caused disease in a member of their residential communities; only 36 per cent of them were demonstrated as sources of new diseases. The disease was most frequently transmitted from sibling to sibling (200), less frequently from father or mother to a child (115 and 112 respectively), much rarer among matrimonial mates (36), and quite rare from children to parents (12 and 7 respectively).—*Tbc.-Exposition und -Erkrankung, F. Wend-*

enburg and Gerken, Beitr. z. Klin. d. Tuberk., November, 1932, lxxxi, 537.—(M. P.)

Bovine-Bacillus Tuberculosis.—It is generally recognized that the bovine type of tubercle bacillus is frequently found in the nonpulmonary forms of human tuberculosis. Koch, in 1908, maintained further that this type of bacillus had never been demonstrated in a case of pulmonary tuberculosis. Since that time several observers have reported cases in which only the bovine type of bacillus occurred in the sputum. The total number of such cases reported from England and Scotland, including those here recorded, is forty-nine. Of these, 45 have been reported during the last 10 years. Thirty-seven of the 49 cases were between 10 and 29 years of age, and 22 were between 17 and 25 years. In no case was there evidence that the disease had been transmitted to another human being. Six of the group had worked on farms and had been in close contact with cattle. It appears, however, that the phthisis in most of these cases is a late manifestation of an infection through the alimentary tract. Between June, 1931, and the end of 1932, the sputum from 222 cases of pulmonary tuberculosis was cultured. In 10 the bovine bacillus was found. All were tested on rabbits and proved virulent. Three of the 10 patients died, and an autopsy was performed in two. In one there was a history of enlarged lymph nodes preceding the onset of phthisis, a fact suggesting that the channel of infection was the alimentary canal. The incomplete autopsy did not permit of definite conclusions. In the second case the disease was confined to the thorax, a fact which suggests that the disease was air-borne. This was quite possible since the patient had worked on a farm and milked cows.—*Pthisis Pulmonalis due to the Bovine Type of Tubercle Bacillus, An Account of Ten New Scottish Cases, A. S. Griffith and W. T. Munro, Lancet, February 25, 1933, ccxxiv, 399.—(R. D.)*

Bovine Tuberculosis and Milk.—The Irish Government's regulations regarding elimination of tuberculous cattle and the inspection of dairy plants has been shown to be unsuccessful. Only cows which are proved to have tuberculous mastitis, tuberculous emaciation, chronic cough, and definite clinical signs of tuberculosis are reported to the local constable for inspection. The inspection is then reported by the constable to the Ministry of Agriculture through the local authority. Tuberculosis is not decreasing. The examination of milk shows an increasing number of samples contaminated with tubercle bacilli. The percentage of contaminated samples rose from 3.5 in 1927 to 8.33 in 1929 in the Belfast area. The problem of eliminating these sources of tuberculosis can be solved by more drastic regulations concerning early detection of the disease in cattle, frequent examinations by full-time veterinarians, more adequate compensation to farmers for their infected cattle, and increased control of local authorities over the purity and cleanliness of the milk sold in their areas. All milk produced should approach the grade-A quality from doubly tuberculin-tested cattle.—*Bovine Tuberculosis and Milk, A. McClean, J. State Med., October, 1932, xl, 597.—(J. F. B.)*

Tuberculosis in Dairymen.—Of 14 cases of pulmonary tuberculosis occurring in those coming much in contact with cattle, 4 were found to be due to the bovine type of the bacillus. Except for one slight possibility, the investigation failed to demonstrate any evidence of an alimentary route of infection in these 4 cases. It would appear that airborne infection with bovine tubercle bacilli does occur in cattle-workers. The possibility of persons discharging bovine bacilli with the sputum and transmitting bovine tuberculosis to animals should be a significant consideration in veterinary practice.—*Pulmonary Tuberculosis in Dairy-Farm Workers and Others Coming Much in Contact with Cattle, W. M. Cumming, Tubercle, February, 1933, xiv, 205.—(T. O. R.)*

Psychological Types in Tuberculosis.—Kretschmer's psychology and "characterology" is a good basis for this largely theoretical discussion of the interplay of tuberculous patients' psychology and disease. Kretschmer distinguishes three main body types: the asthenic, the athletic and the pyknic. As to the psychic constitution, Kräpelin's division of them into the circular and schizophrenic types is acceptable and valuable. Pulmonary tuberculosis has very often been associated with the asthenic constitution. On the other hand the athletic type of constitution has often had acute forms of tuberculosis. It is a general observation that among the pyknic type there are very few cases of tuberculosis, yet this constitutional type is inclined to other pulmonary diseases, such as putrid bronchial catarrh, bronchiectasis and pulmonary abscess. Pulmonary tuberculosis shows a disposition therefore to exist in the asthenic and athletic types, which latter is relatively often associated with the schizophrenic constitution; whereas the pyknic type, relatively often associated with the circular psychic diseases, is fairly immune to tuberculosis. This disposition or immunity to tuberculosis

is, of course, not always present, because too many factors play a rôle which leads to actual pulmonary tuberculosis. Tuberculous individuals are mostly unsocial, humorless, nervous and sensitive, and are book- and nature-lovers, that is, they have schizoid characters, but pure types are not always found. Schizophrenia and tuberculosis are parallel manifestations which have their origin in the same constitutional complex. Tuberculosis may and often does cripple the life-work and cut short the development of the personality, but in artists and scientists tuberculosis apparently does not have any directing influence on their products of art or science. In the case of the asthenic, Chopin for instance, the melancholy of many preludes and nocturnes is compensated by the charm and color of his waltzes and mazurkas. In the case of the tuberculous poet Schiller, there is absolutely no trace of a transposing of his suffering into his works. On the other hand, there may be found sometimes not so much a changed as an increased productivity. Maria v. Weber composed his overture to *Oberon* in the face of death. Molière carried on his stage profession up to the day of death. —*Zur Psychologie der Phthisiker, H. Ulrici, Deutsche Med. Wchnschr., December 16, 1932, lviii, 2003.*—(*H. S. W.*)

Heart in Tuberculosis Patients.—From extensive electrocardiographic and roentgenological studies, it appears that the heart does not play a significant rôle in the development of tuberculosis. The relatively small heart does not in any specific way influence the development of the disease, but the association of a small heart with far-advanced pulmonary tuberculosis, interpreted as a mere coincidence, is unfavorable.—*Das Herz der Tuberkulösen, St. Dedić, Beitr. z. Klin. d. Tuberk., December, 1932, lxxxi, 745.* —(*M. P.*)

Infectiousness of Tuberculous Children.—Opitz and Poulsen have shown that children without clinical evidence of tuberculosis, with the exception of a positive tuberculin test, have frequently tubercle bacilli in the gastric contents. They claim therefore that all tuberculin-positive children are potentially infectious. Clinical observation, however, would indicate that such children are not infectious for other children, although the finding of bacilli in the gastric contents is not doubted. Several careful clinical observations are quoted, which, in conjunction with similar observations from the literature, would indicate that only children with pulmonary tuberculosis who cough are infectious for other children.—*Zur Frage der Ansteckungsfähigkeit der Tuberkulose, R. Priesel, Beitr. z. Klin. d. Tuberk., November, 1932, lxxxi, 570.*—(*M. P.*)

Tuberculosis and Measles.—This study is based on the examination of 20 children with measles, all of whom were known with a reasonable degree of certainty to have been infected with tuberculosis before measles. A positive tuberculin test was obtained in eighteen. In the two who were not tested, necropsy revealed an old tuberculosis. Frequent roentgenograms were made during and after the measles, and in 15 of the cases plates taken before the onset of measles were available for study. The patients could be classified roughly into 6 groups as regards clinical and X-ray findings: *1:* Four cases in which a small area of pulmonary infiltration with hilar adenopathy present before or at the onset of measles showed progressive extension of the infiltration until death ensued 5 days to 4 months after the onset of measles. *2:* Four cases, showing a similar picture in the lungs previous to measles, in whom scattered opacities subsequently appeared in the lung fields, accompanied by dulness, fine râles, and scattered areas of bronchial breathing, as well as further enlargement of the mediastinal shadows. These children were very sick, but in the course of several weeks improved, the physical signs and X-ray findings receding. *3:* Two cases that developed large shadows in the lung following the onset of measles, with little temperature reaction and few abnormal physical signs. These shadows persisted for months, the patients doing well. *4:* Two cases with the so-called primary pulmonary complex. During the measles there was an additional hazy area of infiltration surrounding the site of pulmonary infiltration, from which strands radiated toward the hilar region. This hazy area disappeared entirely within a few days. One of these children died subsequently of tuberculous meningitis. *5:* Four cases in which, in addition to scattered areas of pulmonary infiltration, a pleural effusion appeared during or soon after the measles. One of these children (included also in group 1) died of extensive pulmonary tuberculosis and another of tuberculous meningitis. The other two cases when examined fifteen months after measles still showed some fluid as well as thickened pleura. *6:* Five cases with very little pulmonary infiltration but with enlargement of the lymphatics of the posterior mediastinum and at the bifurcation larger in extent and denser than similar shadows seen in measles in which previous tuberculosis had not been suspected. After the measles these children recovered rapidly, and the size of the hilar shadow decreased. Conclusions of too rigid a nature cannot be

drawn from this study, particularly since roentgenographic interpretation of pulmonary infiltrations is frequently open to error. However, it would appear that in many cases measles does contribute to the spread of a previously existing tuberculous process. In the 6 children that died (5 of whom were autopsied) this deduction could reasonably be made in all but one instance.—*Relation of Measles and Tuberculosis in Young Children: a Clinical and Roentgenographic Study, J. L. Kohn and H. Koiransky, Am. J. Dis. Child., December, 1932, xliv, 1187.*—(*M. D.*)

Splenomegaly in Tuberculosis of Infancy.—Current conceptions as to the frequency, diagnostic significance, and prognostic import of splenomegaly in tuberculosis of infancy are based on data accumulated before the modern diagnostic aids, principally cutaneous tuberculin testing and roentgenography, were fully appreciated. These previous statistics, based mainly on necropsy material, reflected principally the state of affairs in progressive, fatal forms of the disease. The problem was therefore reinvestigated. Five hundred and fifty-seven infants, under hospital surveillance because they had been in contact with tuberculous individuals, were examined for enlarged spleens, greater reliance being placed on palpation than percussion. Of 295 in whom tuberculous infection was not demonstrable, 6.1 per cent had a definite splenomegaly. Of 252 who reacted to tuberculin, 31.3 per cent had enlarged spleens. Many of these had clinically latent tuberculosis, normal pulmonary roentgenograms, and no significant physical findings in their chests. These statistics suggest that the finding of a splenomegaly in an infant, especially in fevers of cryptic origin, should orientate the diagnosis towards tuberculosis. The mortality among the tuberculous infants without splenomegaly (174) was 6.8 per cent, while among those with splenomegaly (79) it was 36.7 per cent. Further, an enlargement of the spleen was present in 70.7 per cent of the 41 cases with a fatal termination. In agreement with the classical teaching, therefore, it is concluded that splenomegaly renders the prognosis less favorable.—*Valeur de la splénomégalie pour le diagnostic et le pronostic de la tuberculose du nourrisson, L. Bernard and M. Lamy, Rev. d. l. Tuberc., October, 1932, xiii, 793.*—(*A. E. M.*)

Tuberculous Infection in Children.—In the city of Trondhjem with a population of 55,000, approximately 5,000 children, 7 to 15 years of age, were tested with tuberculin. Of the total, 23.5 per cent reacted positively, at the age of 7 slightly less than 10 per cent, and at the age of 15 about 40 per cent reacted positively. Comparing these studies with similar ones done by Arnfinsen in 1914 in the same city, it is obvious that the frequency of infection has considerably decreased and that the majority of infections occur now at a later date. The predominant importance of childhood infection does not exist any more. Of children who have lived in contact with open cases of tuberculosis, only about two-thirds reacted positively. Of all infected children, only about 25 per cent had a source of infection in their homes. In reëxamining the children who had been tested in 1914, it was found that an approximately equal percentage of the then negative and positive reactors had developed clinical tuberculosis. It is concluded that a positive reaction at school-age is not a sign of immunity.—*Untersuchungen über die tuberkulöse Infektion im Kindesalter, H. Ustvedt, Beitr. z. Klin. d. Tuberk., November, 1932, lxxxi, 431.*—(*M. P.*)

Tuberculosis in Childhood.—Ten years of work with tuberculous children at the Lymanhurst School has given information in regard to tuberculosis which in some respects is contrary to anticipation. The Pirquet has been supplanted by the more accurate intracutaneous test. It is regarded as a fine screen for tuberculosis. An initial dose of 0.01 mgm. of tuberculin was used and to all who reacted negatively a dose of 1.0 mgm. was given. X-ray examination was relied upon in the search for pulmonary foci, but revealed a questionable to definite lesion in only 22.91 per cent of 4,737 positive reactors. In comparison there was a questionable to definite lesion in 2.79 per cent of 4,031 negative reactors. No tuberculosis of bones or joints was found in the negative reactors, while among the positive reactors 0.52 per cent of such lesions was found. The experience with children under 2 years of age indicates that the prognosis in the positive reactor is good if the infection has not been massive and if the child is removed from further contact with the disease. Only children who have shown the first-infection type (childhood type) of tuberculosis develop the adult and destructive type. It is, therefore, not possible to consider this type of infection as protective to the child. On the other hand, observations on young adults, students and nurses, who became positive reactors following exposure to tuberculosis have shown that they do not develop galloping consumption as was formerly thought. It would appear that the longer the first-infection type of tuberculosis can be prevented in the human body, the better. At Lymanhurst the records have been reclassified according

to the following scheme: *1: Negative to tuberculosis*: These children reacted negatively to 1.0 mgm. of tuberculin and showed no abnormal findings due to tuberculosis. *2: Primary tuberculous infection:* These children reacted positively to tuberculin but showed no discernible lesion. *3: Childhood type of tuberculosis:* (a) Those with the inflammatory stage; (b) those showing calcium deposits. *4: Adult type of tuberculosis:* This includes all of the definite clinical forms of tuberculosis, whether in the lungs or elsewhere. It is felt that the children in group 2 should be recognized as having tuberculous foci and classed as cases of the first-infection or childhood type. An unknown proportion will go on to show lesions which would put them in group 3 or group 4. The childhood type of tuberculosis does not require institutional treatment. Protection from further exposure to tubercle bacilli, good food, conservation of energy, and medical and nursing supervision, such as may be provided in schools for tuberculous children will suffice. When the adult type of tuberculosis does appear special treatment such as collapse therapy is none too drastic.—*Ten Years at the Lymanhurst School for Tuberculous Children, J. A. Myers, Ann. Int. Med., November, 1932, vi, 672.*—(*R. D.*)

Tuberculosis in Childhood.—This study of 60 children with tuberculous pulmonary infiltration has been conducted over a period of five years. From a clinical standpoint the cases were divided into three groups: (1) children acutely ill, with fever, (2) those ailing but not acutely ill, and (3) those with no symptoms but who had been exposed to tuberculosis. All the cases had positive intracutaneous reactions to 0.1 mgm. of tuberculin. In the first group the history was usually that of an acute onset of illness, with high fever and cough lasting 1 to 3 weeks, followed by several weeks of low-grade fever. There were physical signs of consolidation and X-ray evidence of more or less extensive pulmonary infiltration and hilar adenopathy. In this group of 29 children with the picture of tuberculous pneumonia there was only a low degree of toxicity. There were 3 deaths, all under 3 years of age. The others responded well to prolonged sanatorium care, with removal of infected tonsils and adenoids during convalescence. The frequency of tuberculous pneumonia in childhood with a good prognosis has not been generally recognized. The chief symptoms in the second group (18 cases) were anorexia, fatigue, and undernutrition, with occasional short periods of fever and in many instances frequent coughs and colds. There were very few positive chest findings in the physical examination. X-rays showed hilar lymph-node enlargement and relatively small areas of pulmonary infiltration, persisting for many months. These children did well under sanatorium care for varying periods of time, followed by subsequent careful attention to adequate rest-periods at home and at school. In almost half of this group the associated chronic upper respiratory infection played a very definite rôle in the production of symptoms, and removal of infected tonsils was an essential part of the treatment. The third group included 13 apparently healthy contacts who had positive tuberculin reactions. X-ray pictures revealed enlarged mediastinal lymph nodes in about half, and pulmonary infiltrations of varying extent, usually without positive physical signs. Under a careful regimen of afternoon rest, early bed hour, adequate dietary (including codliver-oil), removal of foci of infection, and regular clinical attendance, these cases did well at home, the older children going to school.—*Tuberculous Pulmonary Infiltrations in Childhood, Ann Martin, Am. J. Dis. Child., October, 1932, xliv, 754.*—(*M. D.*)

Tuberculous Laryngitis in Children.—If routine examination of the larynx is performed in children with active pulmonary tuberculosis, it will be found that tuberculous laryngitis is not uncommon, especially in older children. Among 184 children with positive sputum 48 had lesions of the larynx that were considered tuberculous. There are usually no characteristic symptoms, although often there is some loss of tone or huskiness of the voice. Dysphagia and pain are uncommon in children. The condition apparently progresses very slowly.—*Tuberculous Laryngitis in Children, C. D. S. Agassiz, Arch. Dis. Child., October, 1932, vii, 287.*—(*M. D.*)

Epidermal Tuberculin Reaction in Children.—The method which has been recently recommended by Nathan and Kallós was studied on a small group of children. Tuberculin was applied on pads which, covered with oilskin, were fastened for twenty-four hours to the skin. Simultaneously percutaneous tests, according to Moro and Pirquet, and Mantoux tests were done in some cases. It was found that the various tests give similar results and that the intensity of all reactions is the same, regardless of the presence or absence of tuberculosis of the skin. The epidermal tuberculin test in children is of no differential diagnostic value and positive reactions obtained by this method are not characteristic for tuberculosis of the skin.—*Ist die Tuberkulin-Läppchenprobe zur Differentialdiagnose tuberkulose-*

verdächtiger Hautkrankheiten im Kindesalter verwertbar?, P. Seier, Klin. Wchschr., December 3, 1932, xl, 2028.—(K. F.)

Comparative Tuberculin Tests in Children.—Five different types of tuberculin tests were performed within a period of 8 weeks in a group of 55 white children, with active and quiescent tuberculosis, in an effort to determine the comparative diagnostic value of the tests. The intracutaneous test and the "single puncture" test proposed by Stewart (1927) were both positive in 39 children (70.9 per cent), the reactions to the latter method being the smaller in size but equally distinctive. None of this group reacted positively with any other method. For routine office and bedside work the "single puncture" method may be preferred, because it is easier to perform, is less time-consuming, eliminates the necessity for dilution and refrigeration, and is less expensive. The "multiple puncture" method of Craig was found to be somewhat less reliable; the Pirquet and modified Moro (percutaneous) tests were found to be utterly unreliable. —*Results Obtained from the Use of Various Tuberculin Tests, E. Friedman, M. H. Black and A. L. Esserman, Am. J. Dis. Child., January, 1933, xlv, 58.—(M. D.)*

Bronchogenic Tuberculosis in Childhood.—In order to examine the significance of bronchogenic propagation in pulmonary tuberculosis in childhood, 32 cases of childhood tuberculosis, ages nine months to six years, were examined pathologically and histologically. The cause for bronchogenic propagation was excavation of the primary focus in eight, while in two the destructive processes had not as yet produced a true cavity. In 6 cases rupture of a caseated bronchial node into the bronchial tree had occurred. Only 4 cases were typical isolated unilocular phthisis. The bronchogenic foci showed the same two types that were found by Loeschcke to occur in adults: foci due to small seedings and foci due to coarse seedings. Both types are associated in the early phase with circumfocal reactions. Cases of isolated phthisis, that is, without any evidence of haematogenous spread, presented similar pictures as those in adults. Lymph-node caseation was slight, and the lymph nodes did not contain haemorrhagic foci which are almost regularly found in miliary tuberculosis. It is concluded that the source of haematogenous seeding in miliary tuberculosis is lymph-node caseation, as indicated by haemorrhagic areas in these nodes in cases of miliary tuberculosis.—*Untersuchungen über die branchogene Tuberkulose in der ersten Kindheit, L. de Velasco, Beitr. z. Klin. d. Tuberk., December, 1932, lxxxi, 674.—(M. P.)*

Haematogenous Tuberculosis in Childhood.—Of 100 children, up to 6 years of age and coming to autopsy, only 5 had isolated tuberculosis of one organ, 72 had meningitis and miliary tuberculosis, 8 isolated meningitis, and 16 miliary tuberculosis without meningitis. Acute forms may never show a positive tuberculin reaction, and may easily be confused with acute bronchopneumonia. As soon as calcification occurs in the primary lesion, the frequency of meningitis decreases. The more protracted forms of miliary tuberculosis may terminate in chronic cavernous pulmonary tuberculosis. Residual manifestations of healed miliary tuberculosis are disseminated calcified foci in the lung, in the abdominal organs and in the lymph nodes, pleural scars and cylindrical bronchiectases. Residual foci are found predominantly in the apices. Such foci may coalesce to form larger nodules, and they may excavate and initiate pulmonary tuberculosis.—*Die hämatogene Tuberkulose des Kindesalters, G. Simon, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 194.—(M. P.)*

Prognosis of Tuberculosis in Children.—Tuberculosis in infants and children, especially with involvement of the lungs, was formerly given a poor prognosis. It is known now that most children can handle moderate amounts of infection, possibly better than adults, if continuous reinfection is prevented. The three children reported here (aged 15 months, 8 years, and 9 years) all had massive generalized tuberculosis: the first, in the lungs and skin, the second in the lungs, bones, and lymph nodes, and the third in the lungs and bones. They were hospitalized for a period of 1 to 2 years, treatment being heliotherapy and the operative measures indicated by the bone involvement. All three children made good recoveries both from clinical and roentgenological aspects.—*Massive Generalized Tuberculous Infection in Children, with Recovery, L. B. Dickey and Dorothy J. Starks, J. Pediatr., December, 1932, i, 674. —(M. D.)*

Histopathology of Cutaneous and Subcutaneous Nodules in Cattle.—Nodular lesions of the skin and subcutaneous tissues of 50 cattle have been subjected to histological analysis, which revealed three general types of reaction. These are (1) pyogenic abscess, (2) foreign-body pseudotubercle and (3) tuberculous abscess. The pyogenic abscesses were surrounded and separated from one another by considerable fibrous tissue. They contained lympho-

cytes, fibroblasts, budding capillaries, giant cells, caseous and calcified tissue. The foreign-body tubercles were usually small and shot-like. They were situated just beneath the level of the hair follicles. They were conspicuous for the number and syncytial appearance of the giant cells which contained much nonstaining material. Other cells were present, as was fibrous tissue also. The tuberculous abscesses ranged up to 5 cm. in diameter, were often caseocalcareous in nature, were often overlaid by scarred skin, and were surrounded by small tubercles. There was some vascular obliteration but also considerable branching of vessels in the neighborhood of the two types of abscesses. The abscesses were thought to be pyogenic in most instances and tuberculous in a few. It is altogether probable that many of these pyogenic abscesses were originally of tuberculous nature. The specimens came from cattle in six widely separated sections of the United States. Types of lesions were practically indistinguishable among the several groups. Nodules were much more commonly found in the subcutaneous regions than in the skin itself. In tuberculous nodules the skin was involved, especially in the formation of lymphocytic infiltration about the hair follicles, sebaceous glands and vessels. Tuberculous nodules in the skin of cattle do not closely resemble the lesions of lupus in man, from which they differ in their location in the skin, their perivascular origin, peripheral vascularity, and degree of caseation and calcification.—*The Histopathology of Cutaneous and Subcutaneous Nodules of Cattle, R. A. Runnels, J. Am. Veterin. Med Assn., August, 1932, lxxxi (n. s. xxxiv), 173.*—(*H. S. W.*)

Intracutaneous Test for Johne's Disease.—The intravenous method of testing cattle for Johne's disease is laborious and not entirely reliable, and efforts are being made to prepare a tuberculin-like substance from *M. paratuberculosis* which will be applicable intracutaneously in a dependable way. Growth of the bacillus reaches its maximum in four months or more when planted on the synthetic liquid medium recommended by the Wisconsin Agricultural Experiment Station (Beach, *et al.*, 1927). From this an effective *johnin* may be prepared in much the same way that Old Tuberculin is prepared from cultures of tubercle bacilli. The standard dose is 0.2 cc. and the criterion of reaction is the presence of induration at 72 hours after test. This test was applied to 312 head of cattle, of which 41 (13.1 per cent) reacted and 32 (10.2 per cent) gave suspicious responses. Of the 41 reactors 12 were clinical cases, and of the 32 suspicious reactors 6 were clinical cases. More than 60 per cent of these cattle were tested by intravenous injection of *johnin* secured from a commercial house. Of these, 12 (6.2 per cent) reacted to both tests. There was a 28 per cent discrepancy between the two tests. Each test proved to be about equally effective, but when both tests were used together the incidence of reactors much more nearly approximated the incidence of macroscopical disease or demonstration of causative bacteria at autopsy of reacting animals. No acid-fast bacilli were found in 7 reactors to the intracutaneous and in 5 reactors to the intravenous test. And such bacilli were found in several instances in which the animal had reacted to neither test (3 negative to the skin and in 8 negative to the intravenous test).—*An Intradermal Test for Detecting Johne's Disease in Cattle, A Broerman and A. E. Fogle, J. Am. Veterin. Med. Assn., December, 1932, lxxxi (n. s. xxxiv), 795.*—(*H. S. W.*)

Diphasic Nature of Tuberculosis in Rabbits.—The changes in the blood cells following intravenous inoculations of 175 rabbits with tubercle bacilli have been followed. One hundred and forty of these received no treatment and were allowed to die of tuberculosis. The remaining animals were either killed for comparative studies or were given some treatment, in which latter instance no further studies of their blood were included in the analysis. From the group of 140 animals, sections were available for study in 109 instances. The organism used was the B1 bovine tubercle bacillus. All animals were inoculated in the marginal ear-vein, the dose varying from 0.001 mgm. (in four animals) up to 2.0 mgm. Recently 0.1 mgm. has been used as the infecting dose. The rate of mortality showed two definite peaks, one occurring at the end of the first month, and the other at the fifth month, with an intervening period at the end of the third month, when the mortality rate was much lower than the general rate for the entire period. In fact no deaths occurred in the period from 85 to 100 days. The mortality for the whole group (140) is in reality the summation of the mortalities occurring during two separate phases of the disease, and in each instance the distribution of the deaths is typical of an acute infectious disease. With all doses used except the very smallest, a large dose resulted in a greater number of animals succumbing in the first phase of the disease, while a small dose allowed a greater number to survive the first phase. In the case of the animals which received 0.01 and 0.001 mgm., four in each case, all survived the first phase of the disease. The two phases of the disease are

characterized by different pathological findings. In the first three months the spleen, bone-marrow, lymph nodes, and the liver were extensively involved, as well as the lung and kidney. In animals dying after three months, the lesions in the spleen, bone-marrow, lymph nodes and liver were minimal, whereas the lesions in the lung and kidney were extensive. In addition, the lesions in the first three months were most frequently a diffuse infiltration of the organs with a mass of monocytes and epithelioid cells, which showed a tendency to regress without caseation, while in the latter phase the formation of typical tubercles, together with cavity-formation and fibrosis, went on to the exclusion of any other type of lesion. The lesions were now of a chronic nature. During the first phase the changes in the blood cells reflected faithfully the changes in the lesions of each animal as well as for the whole group. As a rule, at the end of the first month there was an anaemia and leucopoenia of all cells except the monocytes. This fall in numbers coincided with the increase of lesions in the bone-marrow. Following the period of anaemia and leucopoenia, the cells tended to return to their previous levels during the second and third months. The monocytes showed a small rise in total number during the first month due to the accession of "stimulated" forms. The stimulated form of monocyte is intermediary between the monocyte and the epithelioid cell. After the first month these stimulated cells decreased somewhat in number and frequency, reappearing during periods of great extension of lesions. The normal monocytes remained at their initial level until the second month, when they rose steadily. For a period of 1 to 2 months before death there was a change in the blood picture of a constant nature. This change was distinguished by a fall in the lymphocytes, steady and continued. During the period of decline the monocytes frequently increased in total number and stimulated forms became more frequent. The close correlation between the maintenance of weight and the maintenance of the lymphocytes, and the simultaneous decline in both suggests that the lymphocytes are either directly or indirectly related to the state of resistance to the disease. In a study of the records of animals which had blood counts done before inoculation it was found that a positive correlation existed between longevity and blood counts of or near the modal value. All of the 66 animals whose records were studied were inoculated with 0.1 mgm. of tubercle bacilli. The relation between longevity and the value of the deviation of the count was most evident in the red blood cells; among the white cells the lymphocytes and the basophiles showed a closer correlation than did the neutrophiles and the monocytes. No direct relationship between longevity and the preinfection ratio of lymphocytes to monocytes could be demonstrated, a very high ratio apparently being as frequently associated with low longevity as a low ratio.—*The Diphasic Nature of Tuberculosis in Rabbits after Intravenous Inoculation with Bovine Tubercle Bacilli, R. M. Thomas, J. Exper. Med., August 1, 1932, lvi, 185.*—(*J. S. W.*)

Bacteriology of Primary Complex.—Different authors have obtained widely divergent results in regard to the presence of viable tubercle bacilli in primary foci. In 157 anatomically healed aerogenous primary foci (that is in their lymph-node component), tubercle bacilli were found in 22 per cent of the cases. The majority of positive findings were obtained in older persons. Iizuka examined 39 primary lymph-node lesions of intestinal infections, and found in histological studies no tubercle bacilli in them. Recent studies of 32 isolated pulmonary primary lesions yielded 21.4 per cent positive findings, all of which originated from cases in the fifth and sixth decades. In 14 anatomically healed primary intestinal lesions no bacilli could be demonstrated. In accordance with anatomical findings, it may be assumed that the primary intestinal infection is less likely to become a source of late dissemination.—*Bakteriologische Befunde bei Primärkomplexen in verschiedenen Lebensaltern, H. E. Anders, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 260.*—(*M. P.*)

Incipient Pulmonary Tuberculosis.—Since the final prognosis of closed cases is infinitely better than that of open cases, all efforts must be directed toward recognizing pulmonary tuberculosis before it becomes open. It was found necessary in this connection to study the mechanism by which closed cases become open. For this purpose 125 cases which became open during observation were studied. In 63 per cent of these the initial prognosis seemed good, in 34 per cent doubtful, and only in 2 per cent bad. Forty-nine per cent of the cases started with exudative foci, 28 per cent showed productive lesions and 8 per cent had calcified or scarred lesions. The interval between first focalization, leading to calcification or scarring, and exacerbation is long and is estimated to be ten to twenty-five years. The exacerbation may start as an infiltrative lesion or it may manifest itself in a slow apicocaudal progression. Activations which develop from exudative lesions usually progress in exacerbations with normal intervals, but these

exacerbations need not be acute, and the intervals may be of considerable length. During the active phases symptoms may be absent and the sedimentation, blood picture and temperature may be normal. The interval between the first diagnosis of a closed lesion and the diagnosis of an open lesion varied between four months and twelve years. In initially productive lesions, the development is slower on the average; otherwise the observable processes are the same. Proper diagnosis is impossible without the use of roentgenological examination. The sedimentation tests were 10 mm. or less in 41 per cent of the patients at the time of the first diagnosis, and in 10 per cent at the time of the first demonstration of bacilli in the sputum. Since about 75 per cent of all patients with open pulmonary tuberculosis are open at the time of the first examination, the question arises whether certain forms of pulmonary tuberculosis are open at the very onset. Completely convincing studies are not available to decide this question, but the available evidence would indicate that most cases are closed for some time before they shed bacilli. A large percentage of those cases that have a positive sputum on first examination gives a history of acute onset. In 12 per cent of these cases bacilli are found with the onset of symptoms, in 65 per cent within three months after the onset of symptoms. The frequency of early open pulmonary tuberculosis in diabetics is stressed, especially in those more than 40 years old. It is calculated that the frequency of this occurrence is 28 times greater than in the nondiabetic population above 40 years. Measures for epidemiological control are discussed essentially in the light of local German conditions.—*Beginn und Verhütung der offenen Lungentuberkulose des Erwachsenen, H. Braeuning, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 12.*—(*M. P.*)

Infraclavicular Infiltration.—This clinical type of pulmonary tuberculosis, described by Asmann-Redeker, as early infiltration, whatever its origin, is a definitely characteristic stage of the disease. It may represent an incipient phase or the reactivation period of a chronic form of tuberculosis. It signifies a critical period when early diagnosis must be made and energetic treatment promptly instituted.—*L'infiltrato precoce di Asmann-Redeker, A. Vignolo-Palombella, Lotta contro la tuberculosi, October, 1932, iii, no. 10, 1078.*—(*U. E. Z.*)

Cavitation in Tuberculosis.—Cavities result from the necrosis of lung tissue. The caseous material is not expectorated as such, but is liquefied, apparently by the secondary infection which occurs when a bronchial communication is established. This period of secondary invasion is marked by exacerbations of fever. There are certain cavities which are symptom-free. The X-ray appearances of cavities in cases persistently sputum-free throughout their illness must be accepted with the greatest caution. Cavities are most wisely treated on their symptomatology and not on their X-ray appearance.—*Cavitation in Pulmonary Tuberculosis, R. C. Wingfield, Brit. J. Tuberc., January, 1933, xxvii, 10.*—(*R. D.*)

Resolving Tuberculous Exudates.—Many cases of pulmonary tuberculosis have been observed and reported in which massive lung shadows have been seen to resolve completely. Some of these are cases of atelectasis due to bronchial compression by enlarged mediastinal lymph nodes; others represent nonspecific pneumonias. In most cases, it is generally agreed, the shadows are due to tuberculous exudates. The majority of workers, however, regard them, not as inflammatory responses to the immediate presence of tubercle bacilli, but rather as toxic or allergic reactions to noxious agents emanating from a neighboring or central "true" tuberculous lesion. A critical review of the cases presented to support such a view indicates that inferences rather than proofs have led to these conclusions, the chief inference, from the pathological standpoint, being that a lesion in the lung which does not show tubercle-formation or the mononuclear exudate of caseous pneumonia is not due to the immediate presence of tubercle bacilli. The author, on the contrary, emphasizes that it is the presence of tubercle bacilli in a lesion which demonstrates its tuberculous aetiology, no matter what the pathological picture. In 2 cases of pulmonary tuberculosis in children, autopsy revealed extensive areas of pneumonia. Aside from scattered areas of caseation, the picture was that of nonspecific bronchopneumonia. Yet a Ziehl-Neelsen stain revealed an extensive distribution of tubercle bacilli in large numbers. That such lesions may completely regress, even though due to the immediate presence of tubercle bacilli, need not be doubted. Experimentally in guinea pigs and rabbits even the classical "norms" of tuberculosis, namely, tubercles and caseous pneumonia, may be completely absorbed. The author suggests that most resolving exudates occurring in the lung in tuberculosis should be designated not by such terms as "epituberculous," "paratuberculous," *etc.*, but as "retrogressive tuberculous pneumonia."—*Resolving Exudates in Pulmonary Tuberculosis in Child-*

hood, H. S. Reichle, Am. J. Dis. Child., February, 1933, xlv, 307.—(M. D.)

Lesions of Dissociated Avian Tubercle Bacilli.—In a preliminary study it was found that the dissociated variants from avian tubercle bacilli were more stable than the variants of either human or bovine cultures. At first three distinct variants were dissociated from the A1 strain (avian) with the following characteristics: *S, Smooth:* Colonies develop slowly, and are smooth and moist on gentian-violet-egg media and have the appearance of half moth-balls. The organisms are easily emulsified in salines. On fluid media these variants grow first in the bottom of the flask, a surface growth appearing only late. *F. S., Flat Smooth:* Colonies are slightly wrinkled, moist, spreading, and from four to six times larger than *S.* The organisms are emulsified with difficulty. On fluid media the growth developed best on the surface. Growth is rapid and profuse on all media. *R, Rough:* On egg media the colonies are large, wrinkled and perfectly dry. The rate of growth is very rapid. On fluid media the organisms grow only on the surface. The fourth variant, *Chromogenic, Ch.* was dissociated from the smooth *S* colonies, which were accidently subjected to a high temperature. The colonies closely resemble the *S* colonies, with the exception that they are chromogenic and ochre in color and are not pathogenic for chickens. The four variants remain fairly stable *in vitro* on proper media. About 80 per cent smooth *S* and flat-smooth, *F. S.*, colonies will develop true to type when cultivated on egg media and about the same percentage of rough *R* and chromogenic *Ch*, when grown on glycerine-agar media. The four variants were inoculated into young fowls and the chickens that died or were killed were carefully necropsied. The blood changes were followed in each case. Attention is called to the fact that the so-called eosinophiles are the predominating granulocyte in the fowl and correspond to the polymorphonuclear neutrophiles present in human blood in their percentage and function. An early nonspecific eosinophilia followed inoculation, no matter what variant was used. This usually subsided in a few hours. The early stages of tubercle-formation produced by all the variants appeared similar. First there appeared aggregations of eosinophiles and their ingested bacilli, soon replaced by large mononuclears which phagocyted both eosinophiles and bacilli. After the formation of tubercles composed only of large mononuclear cells certain differences between the virulent and avirulent variant material became apparent. There was also a certain relationship between the dosage and the extent of the disease. In fowls infected with the *S* variant there was a second rise in the eosinophile count which continued to ascend parallel with the total leucocyte count. The monocytes slowly increased and the lymphocytes diminished. By the third and fourth weeks eosinophiles began to migrate into the centres of the tubercles and abscess-formation became evident. Death usually occurred after 5 or 6 weeks. The appearance of the lesions suggested an acute "toxic" nature of the disease as manifested (1) by marked enlargement of the liver and spleen, (2) by the short fatal course of the disease which never became very extensive, (3) by the presence of few organisms within the tubercles, (4) by destruction of reticulum, and (5) by the marked response of the blood leucocytes. In the group inoculated with the *F. S.* variant the blood counts were similar to the *S* group. During the second week the tubercles showed masses of phagocyted bacilli. The lesions shortly became walled off and there was a rapid increase of bacilli within the tubercle. Necrosis and abscess-formation resulted, accompanied by the dissemination of the organisms both far and near. Wide extension of the disease followed, terminating in death usually within the fifth and sixth weeks. The type of lesion is interpreted as a foreign-body tubercle to distinguish it from the acute toxic nature of the *S* disease. It would seem that the *F. S.* organisms are more resistant to destruction than the *S* organisms, perhaps due to their higher lipin content. A quantitative chemical determination showed that the *F. S.* variant contained 20.14 per cent lipin, whereas in the *S* variant it was only 15.03 per cent. Following inoculation with the *R* variant, the secondary blood change was characterized by an increase of both lymphocytes and monocytes, the latter exceeding the former for a time. Later, usually after the second month, the lymphocytes again became predominant over the monocytes, approaching the normal base-line. The eosinophiles failed to react. This blood-picture indicated a successful resistance against the infecting organism and was supported by the pathological findings. None of the chicks of this group died during the period of study (79 days) although the infecting dose was high. Necropsies on four chicks revealed no macroscopical evidence of tuberculosis. Microscopical lesions were present in the liver and spleen of some cases consisting of discrete clumps of degenerating mononuclear cells often surrounded by a border of lymphocytes. Necrosis, abscess-formation or caseation was not found. Bacilli were not present in the lesions. The chickens injected

with the chromogenic *Ch* variant gave a blood curve similar to the *R* variant, the blood-picture indicating the benign character of the lesions. None of the chickens died, though a dose of 0.5 mgm. was used. Tubercle-formation remained limited to small clumps of two or three large mononuclear cells showing some degeneration. Bacilli could not be found within these tubercles. In three chickens injected with the *S* variant the acute disease became subacute or chronic and the birds survived much longer than others of their group. When cultures were recovered from them, instead of consisting of *S* colonies, they showed the topography of the intermediate type, closely resembling the *F. S.* variant. Evidently this was due to a reversion, that is, a loss of virulence of the organism occurring within the animal body. In planning new tuberculosis studies the different variants of tubercle bacilli must be taken into consideration. With the stabilization of the human-type variants, experiments such as reported above may bring about the proper clinical interpretation of the course of human tuberculosis. Six full-page plates accompany the article.—*Biological Studies of the Tubercle Bacillus. II. A New Conception of the Pathology of Experimental Avian Tuberculosis with Special Reference to the Disease Produced by Dissociated Variants, W. A. Winn and S. A. Petroff, J. Exper. Med., February 1, 1933, lvii, 239.*—(*J. S. W.*)

Pathology of Haematogenous Tuberculosis.—The existence of haematogenous tuberculosis presupposes the occurrence of bacillaemia. Liebermeister was the first to have emphasized the importance and the frequency of bacillaemia in active tuberculosis. He recognized that tubercle bacilli may be present in the blood-stream without causing metastatic lesions. Antibodies are supposed to prevent focalization without, however, destroying the bacilli. There is a group of diseases caused by tubercle bacilli in which, however, the tissue response is not characterized by specific lesions, such as tuberculous exanthemata, phlyctaenulae and probably some rheumatic diseases. In *sepsis tuberculosa gravissima* the foci are usually considerably larger than in miliary tuberculosis, and they are characterized by extensive necroses without a definite defensive reaction of the tissue. Tubercle bacilli are very numerous in the lesions, particularly in the lymphatics. This type of disease presupposes massive haematogenous infection with a low degree of resistance. Tuberculous sepsis occurs under identical conditions as does miliary tuberculosis, but in the latter the body is allergic and in the former it is not. An example is cited of a woman who died of miliary tuberculosis eight days after delivery. Her child died four weeks after birth and showed large necrotic foci in all internal organs and in the lymphatics, but no tubercle-formation in spite of enormous numbers of tubercle bacilli. In contradistinction to tuberculous sepsis, miliary tuberculosis produces foci of small and even size, but the number and density of the foci may differ between the organs of the large and the small circulatory system, depending on the source of the blood-stream infection. Whether the tubercles are more exudative or more productive depends on the duration of the disease. Since all tubercles start with necrosis, followed by exudation and later on by production, it is only the duration of the disease which determines the character of the tubercles seen at autopsy. Weigert's explanation for the blood-stream infection leading to miliary tuberculosis is not acceptable any more, since the intimal tubercles are apparently the results and not the cause of the miliary seeding. However, it must be maintained that miliary tuberculosis is caused by a massive blood-stream infection, since, as mentioned above, single tubercle bacilli do not lead to focalization. Miliary tuberculosis occurs most frequently in Ranke's second stage, because caseated lymph nodes, regularly present in this stage, are the most frequent sources of blood-stream infection. When a caseated lymph node breaks into a vein, the caseated material is washed into the blood-stream, because the capsule of the lumph node prevents the collapse of the node. Other caseated foci, particularly those in the lung, are less frequently the cause of miliary tuberculosis, because the focus and the ruptured vein will collapse after rupture has occurred and blood-stream infection may thus be avoided. While tuberculous sepsis and miliary tuberculosis are undoubtedly haematogenous in origin, the mode of development for other so-called haematogenous foci is doubtful. Single or multiple pulmonary foci may be caused by haematogenous propagation from extrapulmonary foci. The lymph-node reinfection, according to Ghon, is probably an unimportant mechanism for the production of pulmonary foci, since it accounts only for seedings of single bacilli. The apical tuberculosis in young people is frequently claimed to be haematogenous. Since these foci are usually found only when the primary focus is still active and in open connection with a bronchus, it is more likely that these apical foci are bronchogenic seedings. These foci heal rapidly or produce a progressive pulmonary tuberculosis, and they are not the forerunners of apical tuberculosis in adults.

The latter is probably caused by a bronchogenic reinfection. The same mechanism is claimed to cause Puhl's reinfection foci and the so-called early infiltrations. In all cases of early infiltrations which were observed at autopsies, the bronchogenic aspiration from an apical focus could be demonstrated. It is unlikely that early infiltrations are caused by exogenous aspiration, since one must presuppose a more massive infection than could be expected in exogenous infection.—*Die hämatogenen Tuberkulosen.* (*Patholog.-anat. Referat.*), *Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 171.*—(*M. P.*)

Haematogenous Tuberculosis.—Haematogenous tuberculosis may be divided into three main subdivisions: acute haematogenous miliary tuberculosis, recurrent haematogenous seeding with protracted multiple focalization in the large and small circulation, and the single haematogenous seeding which may lead to multiple foci in various organs, which, however, produces more frequently isolated foci in the skeleton or lung. Haematogenous propagation may produce typical X-ray findings in the lung, but the results may be atypical and difficult of analysis. In regard to the clinical symptoms, it must be admitted that they may not differ from other forms of pulmonary tuberculosis. Haematogenous seedings are observed which make practically no clinical manifestations which, however, can be definitely recognized roentgenologically. Their prognosis is always good.—*Die hämatogene Tuberkulose, H. Ulrici, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 183.*—(*M. P.*)

Atelectasis in Tuberculosis.—While plugging of its draining bronchus is the determining cause of atelectasis in any pulmonary area, there are many contributory factors, the most important of which are those which predispose to an accumulation of viscid secretion in the bronchial tree: inflammatory processes in the smaller or larger bronchi; interference with the function of the ciliated epithelium; pain either in the chest or in the abdomen restricting the respiratory effort, and the administration of narcotics to relieve pain which abolish the cough-reflex. Acute lobar or multilobar atelectasis is rarely seen in pulmonary tuberculosis, but it may occur when a bronchus is plugged in the course of haemoptysis. Chronic lobar atelectasis may be seen in infants and children with tuberculous hilar adenopathy when the lymph nodes exert sufficient pressure on a bronchus to interfere with the normal pulmonary drainage. Chronic massive atelectasis in phthisis is usually confounded with extensive unilateral pleuropulmonary fibrosis. The patients usually have a benign course, although their sputum may often show the presence of tubercle bacilli. When respiratory distress develops, patients with chronic massive tuberculous atelectasis can be effectively treated with induced pneumothorax. The pleura in such cases is usually free from extensive adhesions. Lobular or confluent lobular atelectasis is of the most frequent occurrence in all stages of pulmonary tuberculosis. The narrowing of the interspaces, deviation of the mediastinum toward the lesion and elevation of the diaphragm in early cases are not due to fibrosis, which is of slow evolution, but to lobular atelectasis, which develops with great rapidity in any tuberculous pulmonary area. The great frequency of this type of atelectasis in pulmonary tuberculosis indicates that it is one of nature's ways of initiating fibrosis in the involved area.—*Atelectasis in Pulmonary Tuberculosis, B. P. Stivelman, J. Am. M. Ass., November 12, 1932, xcix, 1666.*—(*G. L. L.*)

Massive Collapse in Pulmonary Tuberculosis.—The development of massive collapse of the lungs is reported in two patients with pulmonary tuberculosis of short duration. The collapse in both cases followed a succession of antecedent haemoptyses, the last preceding the signs and symptoms of atelectasis by six days in one case, by two in the other. Apart from an incision of an ischiorectal abscess twenty-four to thirty-six hours prior to the onset of the atelectasis, there had been no operative interference. The diagnosis of massive collapse was made on the basis of physical findings, corroborated by X-ray plates. Reëxpansion of the affected lung began in both patients on the third to fourth day subsequent to the expectoration of a viscous plug of blood-streaked sputum. These cases are illustrative of the mechanism by which massive collapse of the lung may be produced by bronchial obstruction, due in these particular patients to the presence of a bronchial plug of haemorrhagic origin. Similar cases of atelectasis following haemorrhage are reported in the literature among patients in whom the tuberculous infection is of recent occurrence, but only rarely has this complication been found in individuals with a history of long-standing disease. This selective behavior may be explained by the concept that atelectasis supervenes only as the result of two factors, the first the presence of a bronchial obstruction, the second the release of a reflex spasm set up in a healthy bronchus by the foreign body, a power lost in cases of diseased bronchi of long duration. Thus the possibility of massive collapse must be kept in

mind in caring for patients with recent tuberculous disease whenever haemoptyses occur. If pneumonic complications do not develop, atelectasis in itself for a brief period does not carry any grave connotation. Reëxpansion is usually complete.—*Deux observations de collapsus massif aigu atélectasique du poumon consécutif à l'hémoptysie dans la tuberculose pulmonaire, L. Sayé, Arch. Med.-Chir. de l'App Respir., 1932, vii, 43.*—(*V. T.*)

Pathogenesis of Pleural Shock.—The pathogenesis of the syncope, convulsions, and paralysis that occasionally complicate pleural puncture is obscure. The consensus of opinion is that the majority of such pleural reactions are the sequelae of air emboli rather than reflex phenomena. A case is presented which substantiates this point of view. During a reinsufflation of a hydropneumothorax the classical syndrome of pleural shock developed so late and slowly, preceded by prodromal symptoms of bubbling and gurgling sensations perceivable also by the operator, that the almost certain explanation of the signs that followed was that air had been introduced into a relatively large vessel. Fortunately a spontaneous remission of all signs and symptoms took place within thirty-five minutes.—*Embolie gazeuse indiscutable au cours d'une insufflation de pneumothorax. Guérison spontanée, H. Descomps, Rev. d. l. Tuberc., June, 1932, xiii, 616.*—(*A. E. M.*)

Cellular Reactions of Tuberculosis.—The immediate local changes of the tissues in response to the tubercle bacillus resemble very closely the changes that follow other bacterial invasion and are identical with those that occur at the onset of inflammation produced by a great variety of irritants. The tubercle bacillus when first introduced causes scant exudation of fluid and active though transient emigration of polymorphonuclear leucocytes. The cell that later becomes predominant is a mononuclear phagocyte, which in anatomical and functional characters is similar to the mononuclear wandering cells that make their appearance whenever bacterial infection pursues a prolonged course and especially when it proceeds toward recovery. The opinion is expressed that the use of the words "exudative" and "productive" in the classification of tuberculous lesions is open to criticism. The tubercle, according to Baumgarten, is formed in part by proliferation of cells at the site of its formation, and hence has been regarded as productive. Furthermore, the mononuclear cell that constitutes the chief cellular element of the tubercle multiplies by mitosis. The cells and serum that accumulate in the alveoli of the lung with tuberculous pneumonia, on the contrary, are presumably exudative, that is, derived from the blood. This distinction can no longer be maintained, since in the early stage of tubercle-formation there is emigration of polymorphonuclear leucocytes, with other evidence of exudation from blood-vessels. Moreover, mononuclear cells that accumulate in the alveoli also multiply by mitosis and assume the characteristics of those seen in the tubercle. Indeed, it is still uncertain whether the mononuclear wandering cells of tuberculous lesions are derived from wandering cells in the fixed tissue or from similar cells in the blood or from both blood cells and tissue cells, and some still claim that they are derived from the endothelium of small blood-vessels or lymphatics. An intimate union between the fixed tissue of the affected part and the cellular elements that have accumulated under the stimulus of the tubercle bacillus is obtained when reticular fibres make their appearance. The reticulum is coarser at the periphery of the tubercle, where it is continuous with the fibres of the adjacent normal alveolar walls. Later the tubercle is wholly permeated by reticular fibres. When collagen fibrils penetrate the tubercle and tend to replace it, they represent a continuation of the same process. These are reparative changes. It is highly probable that the prolonged course of tuberculosis, with the formation of epithelioid and giant cells, is attributable to the insoluble fat or wax that constitutes a considerable part of the tubercle bacillus and protects it from disintegration. Vorwald has recently described the earliest stages in the formation of the tubercle. At the end of an hour after intravenous injection it is difficult to find tubercle bacilli that have not been taken up by the polymorphonuclear leucocytes in the alveolar capillaries. By this means the tubercle bacilli introduced in the blood-stream are concentrated in small localized cellular masses, which are the ground-work for the development of tubercles. Accumulation is most conspicuous between the fourteenth and eighteenth hour after inoculation. At this time mononuclear cells are infiltrating the polymorphonuclear masses, ingesting the polymorphonuclear leucocytes and taking over the contained tubercle bacilli. After twenty-four hours the focus of cells is predominantly mononuclear. While the tubercle bacilli are multiplying, young mononuclear wandering cells at the periphery of the tubercle are multiplying by mitosis to form epithelioid cells that ingest and destroy the bacilli. When the invading bacilli have been destroyed, mitosis ceases, giant cells appear, and subsequently lymphocytes and

fibroblasts invade the tubercle, and an increasing number of epithelioid cells may be involved. It is noteworthy that the monocytes that form tubercles destroy the tubercle bacilli more effectively than similar cells which have accumulated within the alveoli. In animals reinfected with tubercle bacilli, the initial transient accumulation of polymorphonuclear leucocytes and the subsequent formation of epithelioid and giant cells proceed more promptly and with greater intensity than in previously uninfected animals. Tubercle bacilli are destroyed with greater rapidity in the epithelioid cells of the reinfected animals. After destruction of bacilli, the lesions may undergo partial or complete resolution. There is also much evidence that the heightened inflammatory reaction of animals sensitized by infection with tubercle bacilli promotes the local fixation of reinfecting microörganisms. According to Rich, the retardation of spread may be attributable to a destruction of the bacilli referable to immunization, the heightened inflammatory reaction promoting the accumulation of cellular elements and serum containing antibodies at the site of invasion and destroying rather than fixing the bacilli. The relation of caseation to sensitization, or allergy, is still uncertain. Some writers assume that the number of tubercle bacilli found in association with tuberculous lesions may be too small to explain the occurrence of massive caseation unless the tissue is hypersusceptible to the action of products of the microörganism. It is noteworthy, on the other hand, that the tuberculous lesions produced in animals that have previously been infected with tubercle bacilli and are in consequence highly sensitive to tuberculin, as shown by skin tests, may exhibit much less caseation than those of control animals infected for the first time. The *in vitro* experiments of Rich and Lewis show that cells of the tuberculous animal are peculiarly susceptible to injury by tuberculin. In the living animal, caseation is most likely to occur where epithelioid cells are numerous. Multiplication of tubercle bacilli with continued new formation of epithelioid cells is probably the most important factor in caseation. Under these conditions, sensitization may hasten caseation but it may perhaps occur with no sensitization. In the attempt to define the relation between sensitization and immunity to tuberculosis, the difficulties of measuring immunity are great. The criteria available are resistance to reinfection (always relative, and experimentally determined by prolongation of life or by percentage of recovery) and formation of antibodies, which may have little if any obvious relation to protection against this disease. Sensitization is a phenomenon readily demonstrable in association with some infectious diseases and inconspicuous, if it occurs, with others. There is no evidence that it is essential to protection. Sensitization is inseparably associated with immunity, but since each is dependent on factors peculiar to itself, they do not necessarily proceed parallelly. Experimental evidence shows that sensitization to products of the tubercle bacillus modifies the character of tuberculous lesions and increases the intensity of the inflammatory reaction to the tubercle bacillus, but there is as yet scant information by which the varying character of human lesions can be more exactly interpreted as manifestations of sensitization. The assertion frequently made that frank tuberculous pneumonia is never the result of first infection is believed to be incorrect. It is not improbable that the extent of a tuberculous pneumonia may be increased by sensitization of the tissues, but experimental and human evidence indicates that massive caseous pneumonia is more likely to occur in the absence of previous infection. The apical tuberculosis of adults has the characteristics of tuberculosis in animals made resistant by previous infection. It usually pursues a chronic course, remains localized in the lung and is unaccompanied by caseation of adjacent lymph nodes.—*Cellular Reactions of Tuberculosis and Their Relation to Immunity and Sensitization. General Review, E. L. Opie, Arch. Path., November, 1932, xiv, 707.—(J. S. W.)*

Cellular Reactions to Tubercle-Bacillus Lipoids.—By means of recent biological tests it has been possible to divide the tissue changes in tuberculosis into several parts, for each of which a particular chemical fraction of the tubercle bacillus is responsible. In the present article observations are reported on the effects produced by introducing into the tissues of animals the phosphatides, isolated by the method of Anderson, from five strains of acid-fast bacilli. These were human, bovine and avian tubercle bacilli, the timothy-grass bacillus, and a strain of leprosy bacillus. When it was found that each of the bacterial phosphatides produced similar cellular reactions, attention was directed toward the manner in which these changes were brought about. Observations were then made on the fate of the injected lipoid and the new-formed tissue produced by it. In this way the complete life cycle of the epithelioid cell was determined. Cultures and stains for acid-fast organisms were made, to rule out contamination of the phospholipins by living, dead or partially defatted organisms. Rabbits and guinea pigs were

used in the experiments. The phosphatides were introduced by the intraperitoneal, subcutaneous and intrapulmonary routes. The intraperitoneal route is the one of choice for determining the type of cell affected by the foreign material. The omentum participates most actively in the reaction and is well adapted for the study of either fresh tissue or fixed material. In the intraperitoneal route the usual dose of the phosphatide was 80 mgm. in aqueous suspension. The results are reported largely in tabular form. It now seems certain that the Anderson phosphatides are relatively pure in the biological sense, for no bacteria or fragments of bacteria could be demonstrated by any manner in these substances. In addition the phosphatide was predominantly crystalline when examined under crossed Nicol prisms. The fact that a thin film of phosphatide which has been mixed with water assumed forms which, microscopically, closely resemble degenerating myelin made possible a determination of the fate of this material after injection. The lipoid is phagocytized by monocytes, or, if the stimulus be great enough, by the primitive cells which give rise to the monocytes. Everywhere in the connective tissues of the body are tiny foci of young undifferentiated connective-tissue cells and monocytes. In the omentum these foci are called the milk spots and these areas were specially studied. The life cycle of the cell ingesting the lipoid is as follows: It arises from a primitive cell in the connective tissues (reticular or mesenchymal cell) to pass through the monocyte phase to that of the epithelioid cell. In the latter phase, four distinct stages were observed, namely, that with large irregular vacuoles, that with vacuoles of intermediate but uniform size, that with the smallest, dust-like vacuoles, and the stages of degeneration. Thus, after the lipoid is phagocytized it is subjected to a process of intracellular dispersion into fine particles with the formation of classical epithelioid cells. While this process of phagocytosis and intracellular dispersion is going on, the cells exhibit evidence of proliferation and maturation, it being plain that all the functions of the cell are simultaneously set in action. In every animal receiving the phosphatide there was some caseation. No area was designated caseous unless epithelioid cells could be seen within, or at the margin of, the caseous mass. Less caseation was seen after the phosphatide of the human tubercle bacillus than after the other phospholipins. A comparison was made of the reactions induced by heat-killed and defatted tubercle bacilli with those induced by tuberculophosphatide. The early response to the former was more complex. This is not surprising since both the heat-killed and partially defatted bacilli contain proteins and polysaccharides which cause marked changes in the connective tissues, and which are not contained in the tuberculophosphatide. At a later time the reaction to the heat-killed and defatted bacilli becomes simplified by the disappearance of granulocytes and clasmatocytes, so that the tubercular tissue so produced appears much like that induced by tuberculophosphatide. The phosphatide, which constituted 6.54 per cent of the human tubercle bacillus, is but one of three substances obtainable from these organisms having the capacity to produce epithelioid cells. It cannot, therefore, be expected that the phosphatide will reproduce quantitatively the reaction caused by the same weight of the tubercle bacilli from which it is derived. The phospholipin was injected intracutaneously into two tuberculous animals. The mild reaction obtained was in no way comparable to hypersensitivity to tuberculin. Moreover, animals which had received phosphatide parenterally did not exhibit cutaneous hypersensitiveness to tuberculoprotein. Apparently the phosphatide has no antigenic power. Reproductions of photomicrographs accompany the article.—*The Cellular Reactions to Lipoid Fractions from Acid-Fast Bacilli, K. C. Smithburn and F. R. Sabin, J. Exper. Med., December 1, 1932, lvi, 867.* —*(J. S. W.)*

Accumulation of Iron in Tuberculous Areas.—Experiments were undertaken to determine whether the administration of large quantities of ferric chloride over a long time would increase the survival time of tuberculous rabbits, and to obtain information on the effect of ferric-chloride injections on the development of the tuberculous lesion. Thirty-six rabbits were inoculated with a bovine strain of tubercle bacilli and 16 of this group were given repeated intravenous injections of 0.25 per cent ferric chloride for about 10 weeks. The animals increased in weight during part of the period of these injections. The 20 rabbits that were given no injections were used as controls. The survival time of 10 control rabbits varied from 71 to 124 days, with an average of 94 days. The survival time of 10 experimental animals ranged between 89 and 190 days, with an average of 135 days. The survival time in the experimental group was consistently shifted to a higher level than in the controls. The average increase in survival time of experimental rabbits over that of controls as a result of repeated intravenous injections of ferric chloride was 41 days. Comparison of the tuberculous involvement in the lungs of control and experimental animals indicated that

concomitantly with the accumulation of iron in caseous areas there is a retardation in the progress of the lesions. Studies of weight changes and comparison of the pathological involvement in the lungs of the control and experimental animals at various intervals indicated that the intravenous administration of ferric chloride protracted the course of the disease.—*The Accumulation of Iron in Tuberculous Areas; Effect of Ferric Chlorid Injections on the Course of Development in Tuberculosis in Rabbits, V. Menkin, Am. J. M. Sc., January, 1933, clxxxv, 40.—(W. I. W.)*

Experimental Pulmonary Suppuration.—The results of three series of experiments on rabbits may be summarized as follows: *1:* Those in which pleural adhesions had been produced were submitted to intratracheal insufflation with 2.5 cc. of a 24-hour-old broth-culture of a staphylococcus obtained from a chronic lung abscess. All results were negative. The production of adhesions did not lower the resistance of the underlying lung to a material degree in these experiments. *2:* Cultures made from scrapings of the teeth of a patient with *pyorrhea alveolaris* were introduced into the trachea, and the right lower bronchus was then closed by means of a skin-clip applied from without. The rabbits soon died, and examination showed the blocked lobe to be red and hard like liver. The unobstructed lobes were normal. Less rapid death ensued when cultures of staphylococci were used, but the anatomical findings were the same. The importance of the protection afforded by the power to eject organisms from the lung is emphasized. *3:* In 10 rabbits a fistula was formed between the oesophagus and the trachea. One died two days after operation, in one the fistula closed, while in the remaining 8 diffuse lobular pneumonitis developed, ending in cavity-formation. Three of these animals were fed on sterilized foods and lived longer than the others. Experimentally, the most important factor in the production of abscess of the lung is the inability of the animal to rid itself of particles of moderately septic material deposited on the bronchial and alveolar epithelium.—*Experimental Production of Inflammatory and Suppurative Conditions of the Lung, M. Ascoli and A. Bonadies, Arch. Surg., December, 1932, xxv, 1074.—(R. D.)*

Bronchial Length Changes.—An analysis of bronchial length changes in respiration gives a geometrical picture of the respiratory mechanism at work. A three-dimensional visualization of the bronchial tree in action is attempted, in the hope that it will provide a basis for pathological studies, particularly in the field of tuberculosis. It should make more clear the environmental conditions of the developing tubercle. The associated alterations in bronchial width and certain mass shiftings and peristaltoid movements of the tree are considered with the length changes, and possible clinical implications, concerned with the effects of local or general restriction or abolition of these movements, described. The conclusions regarding bronchial movements have been drawn from direct observation and deduction by means of the X-ray, injection of lipiodol and bronchoscopic examination. A graphic portrayal is given in which the pulmonary framework opens up through the elongation of the bronchial tubes, thus enlarging the interbronchial spaces. The increased space is utilized almost exclusively by the dilated alveolar sacs and ducts. Thus, the entire bronchial tree, from the larynx to the alveoli, must be regarded as extensible and this extension is essential to pulmonary inflation. No part of the lung can be in respiratory action without extension and contraction of the bronchial tree in the region undergoing ventilation. Bronchial action is proportional to the degree of ventilation. There is no evidence in X-ray studies of a swaying movement of bronchi from side to side, or any "angle change." The interrupted nature of the cartilage armature, the loose intervening and enveloping elasticofibrous tissue, the net-like muscle, the slack epithelial layer of the bronchi,—all indicate extension and retraction. The motive force in elongation must be the intrapulmonary air pressure difference which exists in inspiration. When the thorax enlarges, air rushes in along the lines of least resistance, and flows through the conducting part of the tree into the distensible lobules. Stroma enwraps all the distensible lobular tissue. Thus the traction on this stroma induced by the expansion of the lobular tissue extends the bronchi. A recoil movement in expiration is assumed by the arrangement of the elastic fibres of the bronchial tree. The blood-vessels, nerves, lymphatics and interstitial tissue of the lung lengthen synchronously with the bronchial tree to the same degree and by the same mechanism.—*Bronchial Length Changes and Other Movements, C. C. Macklin, Tubercle, October, 1932, xiii, 16.—(M. E. P.)*

Pulmonary Circulation.—W. S. Miller had demonstrated that, although there are no anastomoses between the pulmonary and the bronchial arteries, the bronchial capillaries, partly at least, communicate with the pulmonary venous system. This work was done on dead animals; the authors con-

firmed these observations by experiments on living dogs by injections of colored materials into the pulmonary artery and the aorta, using India ink, carmine red and viridin green. The visceral pleura was found to receive blood either from the bronchial arteries proper or from arteries anastomosing with them, among which are the intercostal, internal mammary and oesophageal arteries. The vasa vasorum of the pulmonary arteries and veins are derived, at least in part, from the bronchial arteries.—*Distribution of the Pulmonary and Bronchial Circulation, C. F. Horine and C. G. Warner, J. Thorac. Surg., October, 1932, ii, 80.*—(*B. B.*)

Autonomic Control of Heart, Lungs, and Bronchi.—The autonomic nervous system mediates impulses which modify the rate and the force of the heart-beats and the conductivity of cardiac muscle. In general, parasympathetic or vagus impulses slow the heart, and sympathetic impulses accelerate it. The relation of the autonomic system to angina pectoris is not yet clear. The autonomic system affects the lungs largely through its action on the bronchi. Vagus stimulation causes contraction of the bronchial muscles, secretion by the bronchial glands, and dilatation of the bronchial vessels. The effects of sympathetic stimulation are the reverse of these. Bronchial asthma apparently results from vagus stimulation, but it is difficult to explain, on this basis, the known benefit of cervical ganglionectomy. There is need for further correlation of the results of animal experimentation and clinical observation.—*The Autonomic Control of the Heart, Lungs, and Bronchi, H. L. Alexander, Ann. Int. Med., February, 1933, vi, 1033.*—(*R. D.*)

Pulmonary Elasticity.—Functional elasticity of the lung is demonstrable, according to Parodi, by its distensibility during inspiratory movements of the thorax and by its retractility during expiration. The author distinguishes between the elasticity due to traction and the elastic reaction of the lung to pressure. The latter is particularly operative in artificial pneumothorax and serves to explain the mechanism involved in selective collapse.—*Sulla elasticita' polmonare, I. Cornia, Tubercolosi, August, 1932, xxiv, 257.*—(*U. E. Z.*)

Basal Metabolism in Pulmonary Tuberculosis.—Estimations of the basal metabolic rate were made 76 times in 76 patients. The rate, based upon the temperature curve, weight curve and anatomical type of lesion, showed no changes which might be regarded as typical of the disease. The variations in the rates appear to be just as changeable as the clinical course of the disease itself.—*Osservazione sul metabolismo basale nella tbc polmonare, M. Moraldi, Tubercolosi, October, 1932, xxiv, 329.*—(*U. E. Z.*)

Effect of Lymphocytosis on Tuberculosis.—It has long been known that individual resistance to tuberculosis is associated with activity of the lymphoid tissues. Cunningham, *et al.*, first called attention to the monocyte-lymphocyte ratio as an index of the progress and extent of the disease. They found lymphopoenia to be associated with poor resistance, and the lymphocytes in the circulation to increase with an increase of resistance. That the state of tuberculous lesions in the tissues is not correlated alone with the number of circulating monocytes is now known. Doan and Sabin recently reported experiments in which they influenced the monocyte-lymphocyte ratio by bringing about a decrease in the number of circulating monocytes, with the result that a greater number of the animals survived into the chronic phase of the disease. It seemed advisable to study the effect of induced lymphocytosis in the course of experimental tuberculosis. The work of Wiseman has made available a simple method of inducing lymphoid hyperplasia. Twenty-five rabbits were used in the experiments and 15 of these served as untreated tuberculous controls. Studies of the blood cells were made for a suitable control period before the animals were inoculated. Five animals received embryonic extract daily, beginning fourteen days before inoculation, and in 5 others the injections were started five days after inoculation. These injections, with one exception, were continued until the death of the animal. The embryonic extract was made from the embryos of fertile eggs which had been incubated for seven days. The amount of extract injected was that derived from one embryo. The organisms used for inoculation were from a ten-day culture of bovine tubercle bacilli, strain B1 grown on egg-meat medium. Each rabbit received 0.1 mgm. (moist weight) intravenously. The necessary controls were inoculated from the same suspension of bacilli. Studies of the blood were made once or twice weekly during the first month after inoculation and once or twice monthly afterward. All differential counts were made with the supravital technique. Autopsies were performed on all animals. *Results:* The blood counts of the animals treated with embryonic extract showed both relative and absolute increases in lymphocytes. In addition, there was an increase in the number of young lymphocytes in the circulation, as well as hyperplasia of the fixed sections of lymph

nodes. After the control period the animals treated with embryonic extract showed lower values for haemoglobin and red blood cells than their specific controls. No other changes of significance occurred in the blood. The average survival after inoculation in the 2 groups of treated animals was 82.7 days, as compared with 114.26 days for the controls. The average survival of any group is less significant than an analysis of death-rates per unit of time, or, more specifically, the distribution of deaths through acute and chronic phases of the disease. However, only 20 per cent of the animals treated with embryonic extract survived more than 100 days, while more than 50 per cent of the controls survived beyond this period. Under the conditions of these experiments an increase in the number of young immature cells in the lymph nodes was accompanied by more extensive tuberculous lesions in the lymph nodes and especially in the germinal centers. A possible analogy to lymphatic tuberculosis in children is suggested. Of the white cells, only the lymphocyte counts are reported. It will be noted that the treated animals showed an increase of lymphocytes from 4,000 to 5,500 on the day of inoculation and the number of lymphocytes continued to rise and reached a peak of more than 8,000 cells nine days after inoculation. After this a decline occurred, but the treated animals continued to show slightly higher average values for lymphocytes than the untreated tuberculous controls.—*The Effect of Lymphocytosis Induced with Embryonic Extract on the Course of Experimental Tuberculosis in Rabbits, K. C. Smithburn, J. Exper. Med., August 1, 1932, lvi, 193.*—(*J. S. W.*)

Pulsatory Movements of Pneumothorax Lung.—A method is described by which the pulsatory movements of a collapsed lung and of the heart can be visualized. The roentgenogram is taken through an opaque screen which has 33 narrow horizontal slits at 12-mm. distance from each other. This screen moves downward during the exposure for a distance of 12 mm. The resultant roentgenogram shows then, due to the discontinuous exposure, corrugated margins of all pulsating organs. By proper correlation of the pulsatory lines, it is possible to analyze which parts of the heart and the large vessels are responsible for the movements of the pulmonary structures.—*Die pulsatorischen Bewegungen des Pneumothoraxrandes, G. von der Weth, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 114.*—(*M. P.*)

Genital Glands and Tuberculosis.—According to Katzmann, the incidence of tuberculosis is greater during the period of sexual maturity and more so in females because full development occurs earlier than in males. Warnekros found that oöphorectomy performed in tuberculous women was followed by marked improvement in their lung disease. In the aged the course of pulmonary tuberculosis is slow and distinctly chronic, with few symptoms of severe constitutional involvement. Morelli calls this the "saprophytic" type of tuberculosis. This particular type of disease occurs after the cessation of sexual life. Six normal rabbits were injected with cultures of tubercle bacilli. Five of the animals died, and at autopsy three rabbits showed definite tuberculous lesions. The average duration of life following the inoculation was 79 days. Six castrated rabbits were similarly injected. The mortality was four out of six and at autopsy none of the animals showed positive tuberculous lesions. The average length of life after inoculation in this group was 108 days. The results obtained would indicate that castration confers upon the animal an increased resistance to tuberculosis. It is suggested that temporary castration by X-ray be attempted in carefully chosen cases. Women between the ages of 30 and 40 years would constitute an ideal group, since most of them will have already contributed their share to maternity and little harm could result. The most suitable cases, anatomically, are the chronic types with slowly progressing and circumscribed lesions.—*Tubercolosi e ghiandole genitali, A. Fabris, Lotta contro la tubercolosi, October, 1932, iii, no. 10, 1047.*—(*U. E. Z.*)

Immunological Reactions in Experimental Tuberculosis.—This work was undertaken in order to establish how soon after an infection an allergic response could be elicited. Infected guinea pigs were reinjected at different intervals, and any change in the development of the reinfection focus, compared with noninfected controls, was considered an indication of an allergic response. It was found that beginning four days after the first infection, a certain immunity is present which is manifested by smaller alterations at the point of reinfection and by smaller lymph-node swellings. The difference between primary and secondary infection increases with the interval between first infection and reinfection.—*Über das zeitliche Auftreten der Immunitätserscheinungen bei experimenteller Tuberkulose, E. Brudnicki, Beitr. z. Klin. d. Tuberk., November, 1932, lxxxi, 579.*—(*M. P.*)

Active Principle of Tuberculin.—In the majority of treatises on the tuberculin reac-

tion it is stated that cutaneous hypersensitiveness to tuberculin cannot be produced by repeated injections of any of the fractions of the tubercle bacillus and that the phenomenon occurs only when there is an accompanying anatomical lesion such as follows inoculation with bacilli, alive or dead. A few suggestions, however, that local sensitization may follow injections of tuberculoprotein stand in the literature. In view of the fact that many investigators have reported good sensitization with protein fractions of tuberculin in uninfected animals, as demonstrated by precipitin titres, active and passive anaphylaxis, uterine-strip contraction and bronchial spasm, it is natural to expect that sensitization could be detected by means of the Arthus phenomenon. The present study is a reinvestigation of the ability of the protein of tuberculin to produce the well-known Arthus reaction. It was facilitated by the possession of this protein in purer and less denatured form and possibly in larger quantity than have been available to previous investigators. A variety of preparations all with tuberculin activity, but made by a number of different methods, were used. T = tuberculin made by growing the human type of tubercle bacillus on Long's synthetic medium for eight weeks and then filtering through Mandler filters. SOT = an Old Tuberculin made in the usual way, but from cultures grown on Long's synthetic medium for weight weeks. O. T. = a lot of Old Tuberculin made in the usual way from cultures of human and bovine tubercle bacilli grown on glycerol broth. TPU = T concentrated by ultrafiltration and purified by continued washing. TPA (impure) = T once precipitated with ammonium sulphate dialyzed from the sulphate and dried. TPA (pure) = T made as described above, but redissolved and reprecipitated many times at pH 4.8, so as to remove as much polysaccharide as possible. This product had 16 per cent nitrogen and 2.8 per cent reducing substances on hydrolysis. TPT = TPU precipitated with trichloracetic acid and containing very little reducing substance. SOTU = SOT purified by ultrafiltration similarly to TPU. SOTT = SOT precipitated by trichloracetic acid similarly to TPT. OTU = OT purified by ultrafiltration similarly to TPU. OTT = OTU precipitated by trichloracteic acid similarly to TPT. Intact human tubercle bacilli (H37) were also used. Antigens were made from the bovine type tubercle bacillus, the timothy-hay bacillus, *B. smegmatis* and *B. butyricus* in the same manner as the impure TPA. Each of two normal male rabbits, weighing 5 pounds was given intravenously every three or seven days, up to 4 or 5 injections, 10 mgm. of the antigen to be tested. Abdominal intracutaneous tests were then made with doses of 15 mgm. of the homologous antigen at weekly intervals, until the animals responded with a typical Arthus reaction, characterized by an oedematous, indurated area, approximately 50 by 50 mm., with a black and red necrotic centre. The results of these experiments showed that repeated injections of TPU, TPA and TPT will sensitize normal rabbits so that they exhibit a typical Arthus reaction when any of these antigens is injected locally, while preparations made from SOT or OT are respectively poorer antigens, those from SOT being less capable of producing sensitization, and those from OT being almost incapable of sensitizing animals and able to elicit only small reactions in highly sensitive animals. Therefore the size of the reaction elicited is first dependent on the degree of sensitization of the animal and secondly on the antigenic capacity of the preparation tested. This apparent antigenic inferiority of OT fractions is not a new finding. An explanation may be found in the fact that both SOT and OT were heated during their preparation. When a correlation is attempted between the precipitin titre and the amount of Arthus reaction obtained in the same rabbit at the same time, no parallelism between the two can be found, as Opie claimed in the case of rabbits sensitized with serum and crystallized egg albumin. The precipitin titres in many cases had reached a maximum when no cutaneous sensitization was evident, and in other cases a high degree of the latter was present accompanied by a low precipitin titre. Several rabbits were tested with the protein of the bovine tubercle bacillus at a time when they were highly sensitive to the homologous protein, and they gave nearly as great reactions. Two of these rabbits and a tuberculous rabbit tested with the protein of the timothy-hay bacillus, the smegma bacillus or *B. butyricus*, gave moderate reactions, but not with the typical necrotic centres. However, when some of these rabbits were tested with crystalline ovalbumin, no reaction resulted. This indicates that there is a portion of the protein common to these different strains of bacilli, but that the sensitization is not merely a nonspecific phenomenon. An attempt was made to transfer passively the cutaneous sensitization occurring in rabbits as a result of repeated injections of tuberculoprotein. Sixty cubic centimetres of serum obtained by pooling the sera from four rabbits, all of which gave a maximum cutaneous reaction to TPA, was heated to 50°C. for one-half hour and then injected into the abdomen of a normal rabbit. The precipitin titre of this serum with either TPA or TPT

was only 1:500. After twenty-four hours, a cutaneous test with 15 mgm. of TPA was performed on this rabbit, and an oedematous reaction 50 by 53 mm. in diameter, with a small necrotic centre, 10 by 10 mm. in diameter, and considerable induration resulted. The rabbit was killed twenty-four hours after the test, and the area excised for histological study. At autopsy, no tuberculous lesions were found. Microscopically, the cutaneous reaction was severe. There were marked oedema and extensive cellular infiltration by polymorphonuclears and mononuclears, with areas of suppuration. Similar results were obtained in a second rabbit treated in the same way. In the next experiments male guinea pigs, weighing from 1 to 2 pounds, were used. All the injections were given intracutaneously at three-day intervals, and in nearly all cases 10 mgm. of the antigen was given at an injection. The results show that it is possible to produce a local cutaneous reaction (Arthus phenomenon) in the normal guinea pig by repeatedly injecting tuberculoprotein with the TPA or the TPT fraction. A reaction with some necrosis may be elicited in some cases as early as the third injection. In these experiments, contrary to those on the rabbit, SOTU did not appear to be inferior as an antigen to TPU, TPA or TPT, all of them producing a maximum reaction by the ninth injection at the latest. OTT, on the other hand, was inferior. However, one guinea pig, made highly sensitive by injections of TPA, responded once with a maximum reaction when the poorer antigen, OTT, was injected locally. It might justly be argued that 10 mgm. is a large amount to be injected intracutaneously into a guinea pig. Therefore 2 guinea pigs which had been rendered highly sensitive to the protein of tuberculin by injections of TPA, were tested intracutaneously with 1 mgm. of the protein. They still exhibited maximum reactions; 0.2 mgm. caused a three-plus reaction, and even 0.1 mgm. caused a two-plus reaction. These tests indicate that normal guinea pigs can be rendered highly sensitive to tuberculin by this method. A comparison of sections of cutaneous reactions to tuberculin in tuberculous animals showed very little difference from the reactions found in the nontuberculous animals sensitized to the protein of tuberculin. Among the normal guinea pigs, never previously given an injection of tuberculoprotein before testicular injection, a few exhibited no testicular reaction whatever, and the others showed a slight intertubular infiltration by polymorphonuclear, eosinophilic or mononuclear exudative leucocytes. All the animals that had been sensitized to one of the tuberculoproteins (TPU, TPA, TPT and SOTU) to such an extent as to give a typical Arthus reaction with the homologous antigen showed intertubular exudation surpassing that in the controls. In most cases, however, the difference in reaction between the sensitized animal and control was slight, not nearly comparable with that seen in the cutaneous reactions. A microscopical study of the spleen was made in a few cases, especially in animals in which the cutaneous sensitization appeared grossly indistinguishable from the cutaneous reaction to tuberculin observed in tuberculous animals. This was done to rule out any possibility of a tuberculosis that may have arisen from the injection of large quantities of the protein fraction, owing to the possible presence of a filtrable form of the bacillus. In none were tubercles found. *Summary:* Specific cutaneous sensitization can be produced in normal rabbits and guinea pigs by repeated injections of the highly purified, undenatured protein of tuberculin. This sensitization is of as high degree and is of the same type as that produced by infection with live tubercle bacilli or by injection of dead bacilli. The most successful methods for preparing and purifying the protein of tuberculin in such a way as to preserve its antigenic capacity were precipitation by means of ammonium sulphate or trichloracetic acid, or merely concentration and washing by means of ultrafiltration.—*Chemical Composition of the Active Principle of Tuberculin. xvi. Local Cutaneous Sensitization (Arthus Phenomenon) Produced in Normal Rabbits and Guinea-Pigs by the Protein of Tuberculin, F. B. Seibert, J. Infect. Dis., November–December, 1932, li, 383.*—(*F. G. P.*)

Tuberculin Proteins and Sensitization.—Tuberculous guinea pigs vary greatly in their sensitiveness to tuberculin, and this factor is of considerable importance in the standardization of tuberculin as well as in many research problems connected with tuberculosis. In a study of the phenomenon three strains of human tubercle bacilli were used, namely, Saranac H37 (virulent) and R1 (avirulent), and no. 119 from the American Type Collection. The last strain is reported to be derived from the original H37. The doses used for sensitizing guinea pigs varied from 0.1 to 2.0 mgm. for H37 and no. 119 and about 20 mgm. for the R1 strain. Guinea pigs inoculated with the R1 strain were found to be the least sensitive to tuberculin (skin tests) and the H37 strain seemed to be the most constant in its ability to induce good sensitization. Strain no. 119 gave variable results. From such observations it seemed that the amount of sensitization elicited might parallel the virulence of the infecting agent. If such is the case, what

property of the more virulent organism would make it a better sensitizing agent? Assuming that the protein element of the bacillus is the sensitizing agent, might not the more virulent bacillus contain a protein which is a better antigen and the avirulent strain a poorer antigen? To test the hypothesis, tuberculin proteins were obtained from raw tuberculins produced by growing the three different strains of tubercle bacilli on Long's synthetic medium. The proteins were isolated by trichloracetic-acid precipitation following ultrafiltration. Equal amounts of these proteins were then used for skin tests in three lots of guinea pigs, each lot sensitized with one of the same 3 strains of bacilli from which the proteins had been prepared,—H37, no. 119 and R1. Regardless of which strain had been used for sensitizing, or what the level of sensitization was for any individual animal, the three proteins possessed the same potency on the basis of their nitrogen content which was approximately the same. The guinea pigs inoculated with the R1 strain continued to show a low degree of sensitization. In fact it required more than a thousand times as much tuberculin protein to produce a maximum skin reaction in these guinea pigs as in the least sensitive guinea pigs of those inoculated with the more virulent strains. Similar proteins were then prepared from tuberculins of the avian and bovine tubercle bacilli and from the timothy-grass bacillus, all grown upon the same medium. When these products were tested in the same guinea pigs used for the former experiment it was found that, in general, with equal doses the largest reactions were obtained with the bovine protein, almost as large reactions with the human (H37) protein, and much less or no reaction with the avian and timothy proteins. However, when large doses were given, as for example a thousand times the usual dose of human tuberculin protein for these guinea pigs, a large reaction invariably occurred with the avian and timothy tuberculin proteins. The fact that the bovine tuberculin protein is more potent than the human tuberculin protein is unexplainable. The conclusion is warranted that the sensitized guinea pig is able to make a quantitative distinction between the proteins of different types of acid-fast bacilli, but is apparently unable to differentiate the proteins from different strains of the same type, such as between virulent and nonvirulent organisms. Speculation, therefore, concerning the course of different degrees of sensitization, must concern itself with factors other than merely the protein itself. Since sensitization is due primarily to the protein of the bacillus, a possible explanation may lie in the question as to whether the degree of sensitization may not be dependent on the amount of protein which is made available to certain cells. That a more virulent form of tubercle bacillus might be better able to bring about such availability is possible. Other factors may be the site of lodgment of the bacilli, or the enhancing effect of substances other than the bacillary protein, such as the lipoids, carbohydrates, etc.—*The Relationship of the Tuberculin Proteins of Different Acid-Fast Bacilli to Sensitization as Indicated by Their Reactivity in Sensitized Animals, F. B. Seibert and N. Morely, J. Immunol., February, 1933, xxiv, 149.—(J. S. W.)*

Tuberculin Reactions and Allergy.—The salient facts of tuberculoallergy are briefly reviewed. True tuberculin sensitiveness probably occurs only in animals sensitized with living or dead tubercle bacilli and, but less consistently, certain complex protein derivatives of them. Histological tubercle alone is not sufficient to induce tuberculoallergy. Purified lipoid extracts of tubercle bacilli will evoke tubercle-formation but not allergy. Neither will they produce cutaneous, ophthalmic, or generalized reactions in sensitized animals. Bing and Kellerman have offered some proof however that *albine*, a diamidophosphatide, does augment the reactivating powers of tuberculin. The question arises whether absorption of tuberculin or tuberculin-like substances from tuberculous foci is a necessary antecedent of tuberculin sensitiveness. The researches of Nicolle and Wolff-Eisner have suggested that such absorption evokes the production of serum lysins which are capable of decomposing tuberculin and liberating an active principle responsible for the inflammatory response. *In vitro* mixtures of serum from tuberculous animals and tuberculin will produce cutaneous and ophthalmic reactions in healthy animals which do not occur when either is injected alone. These reactions have not however been capable of uniform repetition by other observers. It is suggested that tuberculin be rather looked upon as a haptene, which cannot of itself induce the allergic state, but can evoke reactions in animals sensitized by the more complex protein aggregates of dead or living bacilli of which it is only a fraction. Whether tissue hypersensitiveness to tuberculin, which varies in degree in different tissues, is an active or passive phenomenon is a moot point. Keller and Mather have suggested the possibility that cutaneous tuberculin sensitiveness is a nonspecific affair. They obtained transitory reactions to deutero-albumoses in sensitized animals. However, it has been shown that this phenomenon

occurs only if the animals are sensitized by suspensions of artificially cultured bacilli, which suggests simultaneous sensitization to the proteins of the media as the true explanation. Anaphylaxis and allergy, although related phenomena, present definitely distinguishing characteristics. The former is narrowly specific, occurs only after an incubation period of at least seven days, and is characterized by the suddenness and brevity of the shock with death occurring in a few minutes if at all, and with subsequent desensitization if not. Passive transfer is possible. The latter is only relatively specific, may appear as early as three days, the reactions being slow in appearance, lasting and progressive, characterized particularly by hyperthermia and vascular congestion with death, if it occurs, ensuing only after many hours. There is no permanent subsequent desensitization. However, parenterally-introduced extracts of the tubercle bacillus can produce anaphylaxis in animals previously similarly sensitized, but only exceptionally do such animals react to tuberculin. Finally, although allergy in general is associated with a certain degree of immunity against the effects of reinfection, the two are distinct phenomena. Immunity is characterized by a progressive defense ability, by modified cellular activity, fixation of bacilli and their destruction. Allergy is characterized by a local manifestation of inflammation and necrosis of short duration, or a generalized reaction that may terminate fatally.—*Les réactions tuberculiniques dans leurs rapports avec l'allergie tuberculeuse, J. Albert-Weil, Rev. d. l. Tuberc., June, 1932, xiii, 586.*—(*A. E. M.*)

Augmentation of Pirquet Reactions by Adrenalin.—In a previous contribution it was demonstrated that the addition of adrenalin to tuberculin solutions augmented the cutaneous response when tested by the Pirquet technique. The discussion is amplified in the light of new experimental data. The reactions apparently appear no sooner and last no longer, but are often twice as extensive as in the absence of adrenalin. In performing parallel tests, it was found that when tuberculin alone evoked no reaction, the mixture in question likewise yielded negative results. A series of simultaneous tests performed on 32 infants in the first few days of life were all consistently negative. This indicates that the addition of adrenalin does not produce false reactions, and that adrenalin is incapable of inducing tuberculo-allergy, and probably does not augment it. The adrenalin probably modifies the test by increasing the permeability of the cells of the skin and by creating a local peripheral ischaemia, all of which acts to keep a higher concentration of the tuberculin in contact with the cells for a longer period of time. This theory is supported by analagous experiments with methylene-blue in which a longer retention of the dye in scarified skin areas in the presence than in the absence of adrenalin was demonstrated. Clinical interest in this method of tuberculin testing lies in the avoidance of distant focal or general reactions by this method. It is being more generally recognized that tuberculin skin testing is by no means as innocuous a procedure as previously thought. In 13 cases that had had general reactions following skin testing in the customary way, only two had slight rises in temperature and pulse when the above method was used. It is suggested that these ideas are applicable to all skin tests.—*Méthode pour amplifier les cuti-réactions a la tuberculine et pour prévenir les réactions tuberculiniques a distance, A. Bouveyron, Rev. d. l. Tuberc., June, 1932, xiii, 603.*—(*A. E. M.*)

Skin Reactions in Hypersensitive Animals.—It has long been taught that bacteria were the only antigens capable of producing the tuberculous type of allergy (delayed reaction). Recently, however, Dienes has reported it possible to produce, in tuberculous guinea pigs, with ordinary proteins, such as egg-white or horse-serum, a state of hypersensitivity characterized by delayed skin reactions, an absence of demonstrable antibodies in the blood-stream, failure of passive transfer, and insusceptibility to acute shock on intravenous injection. He found that the best method to produce and demonstrate this tuberculin type of hypersensitiveness was to inject the given protein directly into a tuberculous focus and to test the animal within a period of from three to ten days. He concluded that the distinctive characteristics of tuberculin sensitivity do not depend upon some special character of bacterial antigens or upon other secondary factors, but are the result of a special type of sensitization. In the present study microscopical examinations of skin reactions were made, attention being devoted particularly to reactions of moderate or even slight intensity, as it was felt that in these weaker reactions the differences between the early and delayed reactions could be more readily observed. Experiments were carried on in both normal and tuberculous animals, guinea pigs for the most part, occasionally rabbits. At the desired stage of the reaction, the animal was killed and the appropriate skin areas cut out and examined histologically. In the average tuberculin reaction of moderate intensity, a wandering-cell infiltration, predominantly mononuclear in character, was found to occur. This mononuclear predominance was greatest in

the early stage, up to six hours, and again in the late stages from forty-eight hours on. During the intermediate stage the proportion of polynuclears increased but rarely became predominant. During approximately the same period signs of degeneration and necrosis of the epithelium occurred, and the zone of polymorphonuclear infiltration was most intense in the neighborhood of the degenerating epithelial cells. In less severe reactions, the mononuclear predominance was still more marked, and evidence of necrosis could rarely be made out. Tuberculous animals, sensitized and tested with egg-white or horse-serum according to the method of Dienes, also showed on skin test a type of reaction corresponding in every detail of gross and microscopical appearance with the test described above. The passively produced anaphylactic-type skin reactions were in sharp contrast to the above. In such reactions a rapidly developing oedema, quickly followed by a fairly intense polymorphonuclear infiltration, was the first phenomenon observed. This reaction reaches its height somewhere between one and six hours and then rapidly fades away. At twenty-four hours a few persisting mononuclear cells are the only trace of the reaction. In actively produced anaphylactic skin reaction there were also marked oedema and polymorphonuclear infiltration. There was, however, a slight infiltration of mononuclears, evident at six hours and predominant at twenty-four hours. Their number remained far below that seen in tuberculin-type reactions and they failed to show the perivascular and perineural clusters so characteristic of that type. The tendency to selective epithelial necrosis observed in the tuberculin-type reactions was not noted in the anaphylactic type. A study was now made of early reactions in uninfected and tuberculous animals shortly after sensitization, when hypersensitivity was as yet incompletely developed. Skin tests were done within three to six days of sensitization (egg-white or horse-serum). These early tests showed none of the essential characteristics of the anaphylactic type, but resembled tuberculin type of hypersensitivity. They were delayed in appearance, showing nothing grossly before six hours; they persisted forty-eight hours or longer; and microscopically they showed a predominantly mononuclear cellular infiltration in contrast to the polymorphonuclear infiltration characteristic of the anaphylactic type. The reactions observed in uninfected animals did not differ qualitatively from those of tuberculous animals, but were distinctly less intense. In actively sensitized animals a certain amount of the tuberculin type of hypersensitiveness develops along with, or persists as an underlying factor in, the stage of anaphylactic hypersensitiveness, so that what we are observing is really a mixed reaction with a predominance of the anaphylactic type. *Conclusions: 1:* The tuberculin type of hypersensitiveness represents the first stage of the immune response to parenterally introduced protein antigen. *2:* It occurs in uninfected as well as in tuberculous animals. *3:* A tuberculous infection quantitatively increases it, but does not alter it qualitatively *4:* It may be demonstrable as early as the third day after sensitization.—*Histological Studies of Hypersensitive Reactions. Part I. The Contrast between the Histological Responses in the Tuberculin (Allergic) Type and the Anaphylactic Type of Skin Reactions. Part II. The Tuberculin (Allergic) Type of Response in the First Period of Sensitization and Its Relation to the Process of Immunization, L. Dienes and T. B. Mallory, Am. J. Path., November, 1932, viii, 689.*—(*J. S. W.*)

Relationship of Allergy and Immunity in Tuberculosis.—The term *allergy* is not well defined. Allergy is the acquired specific hypersensitiveness to tubercle bacilli, but the term frequently is used for the acquired reactivity to tuberculin. It seems preferable to include the acquired hypersensitiveness as well as the acquired specific anergy, since the latter too is a phenomenon of immunity. The significance of the nonspecific defensive mechanism was completely disregarded by Behring and Roemer when they advanced the theory of the overwhelming influence which spècific immune bodies exert on the development and course of the tuberculous disease. With Lydtin, Lange was able to demonstrate that in accordance with Koch's classical experiment, the degree of immunity is running parallel to the extent and the intensity of the tuberculous process. Patients with latent tuberculosis and a marked tendency to healing show a low-grade specific immunity and cases with a progredient lesion have as a rule sharp immunity reactions. A massive or virulent infection confers a stronger immunity than the treatment with attenuated strains. These facts, which are not in accordance with prevailing views, that clinical improvement goes hand in hand with a high-grade immunity or progrediency with the lack of specific antibodies, suggest that development and course of the tuberculous disease depend to a great extent on other nonspecific factors. It is generally assumed that the striking differences in the reaction to the primary infection is caused by variations in the infecting dose; these differences, however, are better explained by the varying individual resistance because the infecting dose in direct infection of the lungs by inhalation

is always minimal. It is therefore extremely difficult to determine on the basis of clinical observations alone the extent to which the course of the infection is influenced either by the acquired specific immunity or more by the natural resistance of the individual. Animal experiments indicate very strongly a close relationship of hyperallergic phenomena to tuberculoimmunity. Both are noticeable as soon as tuberculous foci develop and persist only as long as foci with living tubercle bacilli are present in the host. The parallelism of allergy and immunity in tuberculosis had been recognized by Koch. In his experiments, however, the manifestations of immunity were obscured by allergic phenomena because too heavy doses were used for superinfection, and later investigators only discovered the important fact that depending on the mode of reinfection either allergy or immunity may predominate. Calmette and Guérin for instance found in cattle and Roemer likewise in sheep a strong allergy developing immediately after intravenous reinfection, whereas, much later, a marked inhibition of the formation of tuberculous tissue can be noticed. Many observations suggest that allergy does have in a certain sense immunizing effects. The local reaction at the site of injection of antigen which may run the gamut from a slight infiltrate to oedema, necrosis and ulceration can be interpreted as a protective process since the capillary stasis and the oedema tend to prevent the rapid absorption of antigen. Krause and Willis could, in fact, demonstrate that the allergic reaction fixes tubercle bacilli at points of reinfection and thus prevents or retards their spread. If smaller doses similar to those causing reinfection by inhalation in human beings are used protection against reinfection without allergic symptoms at the point of reinoculation can be noted. The intensity of the tuberculin reaction bears no relation to immunity and the skin anergy which has been observed after intercurrent infectious diseases does not necessarily prove that immunity has broken down. It must be assumed that both the anergic and the allergic reaction have protective effects in the defense against reinfecting bacilli, but it is impossible to define clearly the relationship of allergy to immunity in tuberculosis until we have a better knowledge of both phenomena.—*Die Beziehungen zwischen Allergie und Immunität bei der Tuberkulose, B. Lange, Klin. Wchschr., December 3, 1932, xi, 2017.*—(*K. F.*)

Meningeal Hypersensitiveness in Tuberculous Animals.—The hypersensitive state may be of significance in the pathogenesis of certain central-nervous-system disturbances. In the first study of this phenomenon tuberculous animals were employed because it is known that their tissues are sensitive to tuberculin. The subarachnoid space was chosen as the site of study because of its accessibility through the basal cistern and, furthermore, because of its very intimate relationship with the cerebral parenchyma. Guinea pigs, averaging 200 to 300 gm., were used in the experiments. These were inoculated subcutaneously with a light suspension of virulent human tubercle bacilli. The tuberculosis in the animals was allowed to progress to various stages before the test-inoculation was made. Old Tuberculin and living and killed tubercle bacilli were the test-agents. Not more than 0.2 to 0.3 cc. of solution can be safely inoculated into the basal cisterns of the animals. The technique of inoculation is fully described. Every experiment included control animals. The tuberculous controls had glycerine-broth inoculated. The nontuberculous controls were inoculated with Old Tuberculin and glycerine-broth. In preliminary experiments the nature of the response and the type of the lesion produced in the central nervous system by the inoculation of tuberculin in tuberculous animals was determined. Within 4 to 5 hours after inoculation of tuberculin into the cisterns, restlessness and ruffing of hair appeared, which became progressively more severe until twitchings and convulsions resulted. Marked weakness, incontinence and opisthotonus were followed shortly by death which occurred within 6 to 12 hours. The tuberculous animals receiving glycerine-broth, as well as the nontuberculous animals which received tuberculin, never showed any clinical evidence of cerebral irritation. In the subarachnoid space of the tuberculous animals receiving tuberculin an extensive exudate developed which extended over the convexities of the brain and into the sulci. There was no histological evidence of damage to the cells of the cerebral parenchyma. The control animals showed either a very slight nonspecific reaction or none at all. Tuberculous animals, that received the glycerine-broth *via* the cisterns, always responded with a very slight nonspecific type of reaction. Since guinea pigs with far-advanced generalized tuberculosis uniformly developed the most widespread exudate in the subarachnoid space in 8 to 12 hours, it was possible to take this time as the maximum period after the inoculation of tuberculin for killing and examining the animals. In a series of tuberculous guinea pigs at designated intervals two were selected from the group and each received 0.3 cc. of 1:100 dilution of tuberculin in physiological salt solution *via* the cisterns. If the animals did not develop symptoms and

die before 12 hours they were filled. Those receiving tuberculin as early as 5 days after the initial infection, at a time when they gave a negative skin test, reacted with a slight but definite exudate at the base of the brain, distinctly more than a nonspecific response. By the fourteenth day definite clinical symptoms followed the tuberculin inoculation and an extensive exudate developed in the sulci. At 24 days the animals died within 6 hours. By this time the animals had developed definite visceral tuberculosis with macroscopical tubercles in the lungs and spleen. These results indicate that the degree of response of the central nervous system tissues to tuberculin is directly related to the extent of the visceral tuberculous disease. In further tests a higher dilution (1:1000) of tuberculin was employed which permitted the animal to survive longer than 24 hours. Here the exudate formed in the sulci and at the base of the brain it was characterized by small lymphocytes, whereas in those in which death had occurred in from 6 to 12 hours the exudate was distinctly polymorphonuclear. The intensity of the response is also proportional to the dose of tuberculin employed. In order to bring the tuberculin into closer contact with the ganglion cells of the cortex, the skull was trephined and the needle inserted directly into the cortex and the material injected. The response was similar to the reaction obtained by cistern injection. Both living and dead tubercle bacilli were next tested to determine the response of the leptomeninges in hypersensitive animals. Concentrated living bacilli elicited a very vigorous response. The animal that survived for a period of 10 days showed an exudate and proliferative type of response. There were many tubercles throughout the perivascular spaces of the brain. When minute quantities of living tubercle bacilli were inoculated the response was mild, and the infiltration and exudate lymphocytic in character. Tubercles were rare. The same dosage of bacilli in the control (normal) animals resulted in marked tubercle-formation throughout the cortex and meninges. In 3 allergic animals dead bacilli, in the same concentration as the heavy suspension of living bacilli used, elicited a definite response in the meninges with death within 4 to 12 hours. The results of these experiments, together with the fact that most if not all cases of tuberculous meningitis are secondary to some primary focus in another part of the body, assuredly indicate that a state of allergy exists in the subarachnoid spaces before the bacillus reaches the boundaries of the brain or its coverings.—*The Rôle of Hypersensitivity in the Production of Experimental Meningitis. Experimental Meningitis in Tuberculous Animals, C. G. Burn and K. H. Finley, J. Exper. Med., August 1, 1932, lvi, 203.*—(*J. S. W.*)

Lethal Effects of Fresh Cow-Serum.—Doses of more than 1 cc. of fresh serum from cows being immunized against *Brucella abortus* were noted to be fatal to guinea pigs when injected intraäbdominally. Subcutaneous injections gave rise to slight nervous manifestations, but there was marked local reaction with sloughing of the skin. Fresh cow-serum was added to 1 cc. of a suspension of washed guinea pig cells in 0.85 per cent sodium-chloride solution, in quantities of 0.01, 0.1 and 1.0 cc., and placed in a water-bath at 37°C. Haemolysis was not produced in the most dilute solution. Fresh serum, heated to 56°C. for thirty minutes, did not produce haemolysis, nor did serum nine days old. Fresh cow-serum haemolysed human, rabbit and sheep cells but at a slower rate. Fresh cow-serum cannot be injected into guinea pigs without danger.—*Fatal Results in Guinea Pigs Following Intra-abdominal Injection of Fresh Cow Serum, R. Gwatkin, J. Am. Veterin. Med. Ass., August, 1932, lxxxi (n. s. xxxiv), 250.*—(*J. F. B.*)

Recent Research in Biology of Tubercle Bacillus.—This is a brief review of recent work in the biology of the tubercle bacillus, comprising such items as life-cycle, filterable phases, virulence and dissociation. It is concluded that there is no convincing evidence that the tubercle bacillus may occur in any other form than the classical Koch type. There are real advances in the isolation and culture of the tubercle bacillus. Renewed studies of the pathogenicity of bovine bacilli for human beings have proved that this type is quite pathogenic for man. But the most frequent way in which human beings are infected is by inhalation infection with very few bacilli.—*Neuere Forschungen zur Biologie des Tuberkelbacillus, B. Lange, Beitr. z. Klin. d. Tuberk., October, 1932, lxxxi, 235.*—(*M. P.*)

Growth of Tubercle Bacilli within Single-Celled Organisms.—In this study an attempt was made to investigate further the problem that has been raised as to why some human monocytic cells support the growth of tubercle bacilli while others do not. The ideal procedure would be to cultivate tubercle bacilli and monocytes together, modifying the chemistry of the media so that multiplication would or would not occur. However, the culture of tissue is in itself such a delicate procedure, requiring such complicated media, that this appears to be an

unsuitable method for an experiment in which the environment of the cell must be modified chemically. In the search for a unicellular form suitable to the experiment in view it was found that the *Colpidium campylum* would both grow in sterile laboratory media and tolerate the desired environmental changes. Tubercle bacilli from man and cold-blooded animals were ingested by the cells of a pure culture of this ciliate in peptone-dextrose and peptone-glycerol media. No evidence of multiplication of the tubercle bacilli within the cells could be detected in either medium, in spite of the well-known favorable influence of glycerol on the growth of tubercle bacilli. Extrusion of the bacilli appears to be one of the end-results of their ingestion. Bacilli were found in close association with the excretory stuffs of the colpidia, usually from four to nine days after the inoculation of cultures of *Colpidium campylum* with tubercle bacilli. Digestion of the tubercle bacilli is another possible end-result of ingestion. Bacilli ingested by the cells in certain instances appeared to be digested intracellularly, formless masses of acid-fast material being found in the probable intermediate stage. The work definitely suggests that the colpidium can live at least a number of days in association with ingested bacilli, ridding itself of some or all of them by digestion or extrusion.—*An Attempt to Grow Tubercle Bacilli within the Single-Celled Organism Colpidium Campylum, L. E. Jordan, J. Infect. Dis., November–December, 1932, li, 482.*—(*F. G. P.*)

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